

Metformin increases pathologic complete response rates in breast cancer patients with diabetes

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Metformin, the common first-line drug for type 2 diabetes, may be effective in increasing pathologic complete response rates in diabetic women with early stage breast cancer who took the drug during chemotherapy prior to having surgery, paving the way for further research of the drug as a potential cancer therapy, according to researchers at The University of Texas M. D. Anderson Cancer Center.

The retrospective study is the first clinical research observation of the diabetes drug as a potential anti-tumor agent. The findings will be presented in a poster discussion session at the annual meeting at the American Society of Clinical Oncology (ASCO) by Sao Jirlerspong, M.D., Ph.D., a fellow, and Ana M. Gonzalez-Angulo, M.D., assistant professor, both in M. D. Anderson's Department of Breast Medical Oncology.

Metformin, an oral medication, is the most common drug prescribed for type 2 diabetes; according to Gonzalez-Angulo, more than 35 million prescriptions of the drug are filled annually. It's most often given to diabetic patients who are obese or have insulin resistance.

The authors decided to conduct the research after a large, intriguing epidemiologic study published last year showed that patients with diabetes who took metformin had lower incidences of cancer as well as better outcomes.

"Metformin has a novel mechanism of action. There have been a number of papers published recently that describe its action through activation of the AMP kinase pathway, which is a cellular energy sensor of the cells and potentially important pathway for the development of cancer," said Jiralerspong.

"The other interesting aspect is that Metformin works by decreasing the amount of insulin- resistance in diabetics and insulin seems to be a growth factor for cancer," said Gonzalez-Angulo.

Using the M. D. Anderson Breast Medical Oncology database, Gonzalez-Angulo, Jiralerspong and their team identified 2,529 women with early-stage breast cancer who received chemotherapy in the neoadjuvant setting, before surgery. Of the patients, 2,374 were non-diabetic, 68 were diabetic but not taking metformin and 87 were diabetic and taking the drug. The study's endpoint was pathologic complete response, or the absence of cancer at the time of surgery.

The researchers found that the pathologic complete response rates in the diabetic breast cancer patients taking Metformin was 24 percent, three times higher than the rates in diabetic patients not taking the drug, 8 percent. In the non-diabetic women, the pathologic complete response rate was 16 percent. After adjusting for other factors, the researchers found that metformin was an independent predictor of pathologic complete response in diabetic patients.

While very exciting, the findings are still very early, cautioned Jiralerspong and Gonzalez-Angulo, and further investigation with metformin is needed.

"We need to study the mechanism of the drug - perhaps it's the decrease in insulin levels, or it may be that the drug has an anti-tumor effect that we to look at in vivo," said Gonzalez-Angulo. "Our next step is to

conduct a number correlative studies to try and further understand its mechanism."

M. D. Anderson also plans to open a clinical trial with metformin in combination with hormonal therapy for metastatic breast cancer patients who are obese. The study will be led by Francisco Esteva, M.D., Ph.D., associate professor in the Department of Breast Medical Oncology.

Source: University of Texas M. D. Anderson Cancer Center

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