First in-human trial of endoxifen shows promise as breast cancer treatment

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A Phase I trial of endoxifen, an active metabolite of the cancer drug tamoxifen, indicates that the experimental drug is safe, with early evidence for anti-tumor activity, a Mayo Clinic study has found. The findings indicate that Z-endoxifen, co-developed by Mayo Clinic Cancer Center and the National Cancer Institute (NCI), may provide a new and better treatment for some women with estrogen positive breast cancer and, in particular, for those women who do not respond to tamoxifen and aromatase inhibitors. Results of the first in-human trial were presented today during the 2013 San Antonio Breast Cancer Symposium.

"We achieved up to 60 fold higher levels of endoxifen compared to endoxifen levels achieved with the standard dose of tamoxifen," says Matthew Goetz, M.D., a Mayo Clinic oncologist and lead author of the study. "We have seen evidence for tumor regression in patients who had failed standard hormonal therapies including aromatase inhibitors, fulvestrant and tamoxifen. This is an exciting first step in the development of this drug."

Tamoxifen is a hormonal therapy that has been used for over 40 years to reduce the risk of breast cancer recurrence and to prevent breast cancer. Some prior studies have demonstrated that patients with very low levels of a critical enzyme called CYP2D6 and those with low endoxifen concentrations have a higher risk of recurrence or progression when treated with tamoxifen. In 2008, Dr. Goetz and Matthew Ames, Ph.D. at the Mayo Clinic Cancer Center began to collaborate with the NCI to develop formulations of endoxifen. This formulation, known as Z-endoxifen hydrochloride (endoxifen), was tested through preclinical pharmacology studies, toxicology workups and, most recently, clinical trials conducted at Mayo Clinic and NCI.

In the Phase I study, researchers gave endoxifen once daily to 22 women with estrogen-receptor positive breast cancer that was resistant to standard hormonal therapies such as aromatase inhibitors, tamoxifen and fulvestrant. The drug appeared to be safe even at the highest dose of 160 milligrams/day.

Dr. Goetz and his colleagues are now working to determine the optimal dose of endoxifen for breast cancer patients. After that work is complete, Dr. Goetz would like to see the drug studied in premenopausal patients where tamoxifen is the only FDA approved hormonal agent for the treatment of estrogen receptor positive breast cancer. "Endoxifen may turn out to be a better drug than tamoxifen," he says, "and not just in patients who have limited CYP2D6 metabolism. This is something that has to be prospectively tested."

Provided by Mayo Clinic