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# Estrogen receptor status of HER2+ breast cancer correlates with response to anti-HER therapies

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An international team of researchers has discovered molecular evidence that may explain why some women with HER2 over-expressing breast cancer do not respond to drugs designed to target this important molecule.

The research, presented at the IMPAKT Breast Cancer Conference in Brussels, Belgium, could have an important impact on future clinical trial design and treatment strategies in HER2 over-expressing breast cancer.

The over-expression of HER2 --a molecule found on the surface of cells-- is an important marker in breast cancer. It had been associated with a poor outcome for women, but with the advent of anti-HER2 targeted agents, the prognosis for these women has improved.

But oncologists have known for some time that some HER2 over-expressing (HER2+) breast cancers do not respond to trastuzumab, currently the most commonly prescribed anti-HER2 agent.

Belgian and US researchers led by Dr Sherene Loi from the Institute Jules Bordet in Brussels set out to determine whether estrogen receptor status, another major biological variable in breast cancer, was involved.

"We looked at HER2+ breast cancer using gene expression data, array

comparative genomic hybridization, cell lines and clinical data from nealry 2000 patients to determine if estrogen-receptor status plays a significant part in the biology of HER2+ breast cancer and response to anti-HER2 therapies," said Dr Loi.

"We found that estrogen receptor status of HER2+ breast cancer seems to be correlated with different responses to anti-HER therapies. Currently, the biological differences in the group of breast cancers that overexpress HER2 are largely unknown."

The results show that patients with ER+/HER2+ compared with ER-/HER2+ breast cancers may actually benefit more from drugs that inhibit the PI3K/AKT molecular pathway, as this could be the dominant biological pathway for tumor growth and progression, the researchers say.

"In contrast, our data suggest that inhibition of estrogen receptor --alone and in combination with such an inhibitor—could actually result in a worse outcome for the patient," Dr Loi adds. "This may help explain why researchers saw such a poor outcome in clinical trials where women with HER2+ cancer were given hormonal therapy alone."

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