New type of drug shrinks primary breast cancer tumors significantly in just 6 weeks

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A drug that targets the cell surface receptors that play an important role in many types of cancer can bring about significant tumour regression in breast cancer after only six weeks of use, a scientist told the 6th European Breast Cancer Conference (EBCC-6) today. Dr. Angel Rodriguez, from the Lester and Sue Smith Breast Center, Baylor College of Medicine, Houston, USA, said that the work demonstrated for the first time that the tyrosine kinase inhibitor lapatinib could decrease tumour-causing breast cancer stem cells in the primary breast cancers of women receiving neoadjuvant treatment (treatment given before the primary surgery for the disease).

Dr. Rodriguez and colleagues studied 45 patients with locally advanced breast cancer in which the gene HER-2 was over-expressed. The patients received lapatinib for six weeks, followed by a combination of weekly trastuzumab and three-weekly docetaxel, given over 12 weeks, before primary surgery. Biopsies were performed at the time of diagnosis and also after six weeks of lapatinib and cells from the tumours were obtained and analyzed.

“We saw significant tumour regression after six weeks of single agent lapatinib,” said Dr. Rodriguez. “Bi-dimensional tumour measurements showed a median decrease of minus 60.8%. We had previously showed that tumour-causing breast cancer stem cells were resistant to conventional preoperative chemotherapy; indeed, residual cancers that were exposed to such chemotherapy showed an increase in tumour-causing cells and enhanced tumour initiation by the formation of

mammospheres, small tumours that form when tumour-causing cells are cultured in a test tube, which reflect the capacity of the cells to self-renew. So we were excited to see that the results with lapatinib were different."

Dr. Rodriguez's results suggest that specific signalling inhibitors of the pathways responsible for stem cell self-renewal could provide a possible therapy for eliminating tumour-causing cells in order to achieve the long-term eradication of cancer.

Cancer stem cells help maintain the malignant tissue in the tumour by regenerating the tumour after attack from chemotherapy drugs. "This indicates that the stem cells themselves should be the specific target of chemotherapy drugs," said Dr: Rodriguez. "Rather than the broad brush approach, in which cells are killed indiscriminately, targeting the stem cells may be more effective and also prevent some of the unpleasant side effects associated with conventional chemotherapy treatment."

Scientists believe that cancer stem cells come into being through damage to their own DNA, which affects the regulation of their self-renewal. Other cells divide into two 'daughter' cells, but a stem cell can divide into a new stem cell and a 'progenitor' cell. The progenitor cell loses the power of self-renewal, but can still change into the cell type of the tissue served by the stem cell. The stem cell population then continues to renew itself as it generates new cells for the tissue. "This means that, unlike other cells, the stem cell has lost control over its own population size," said Dr. Rodriguez.

Lapatinib has few side effects, and those that exist are minimal, including diarrhoea and acne. But it is expensive. "In the US it costs between $2000 and $3000 a month," he said.

"This is an exciting finding, and we will be starting further studies on

stem cells in order to confirm it. We will also look into its applicability in testing novel agents targeting tumour-initiating cells. This finding should also apply to other types of cancers and research of tumour-initiating stem cells in other cancers is ongoing," said Dr. Rodriguez.

"International studies are currently underway looking at the effect of lapatinib in lung, colon, head and neck, gastric, oesophageal, and bladder cancer and lymphoma, among others," he said.

Source: ECCO-the European CanCer Organisation

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