S22. Prevention of ER-negative breast cancer

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The successful demonstration that the selective estrogen receptor modulators (SERMs) tamoxifen and raloxifene reduce the risk of breast cancer has stimulated great interest in using drugs to prevent breast cancer in high-risk women. In addition, recent results from breast cancer treatment trials suggest that aromatase inhibitors may be even more effective at preventing breast cancer than are SERMs. However, while SERMs and aromatase inhibitors do prevent the development of many ER-positive breast cancers, these drugs do not prevent ER-negative breast cancer. Thus, there is an urgent need to identify agents which can prevent ER-negative breast cancer. We have studied the cancer preventive activity of several classes of drugs for their ability to prevent ER-negative breast cancer in pre-clinical models. Results from these studies demonstrate that rexinoids (analogs of retinoids that bind and activate RXR receptors), tyrosine kinase inhibitors (such as EGFR inhibitors and dual kinase inhibitors that block EGFR and HER2/neu signaling), and cyclo-oxygenase 2 (COX-2) inhibitors all prevent ER-negative breast cancer in transgenic mice that develop ER-negative breast cancer. Other promising agents now under investigation include vitamin D and vitamin D analogs, drugs that activate PPARgamma nuclear receptors, and statins. Many of these agents are now being tested in early phase cancer prevention clinical trials to determine whether they will show activity in breast tissue and whether they are safe for use in high risk women without breast cancer. The current status of these studies will be reviewed. It is anticipated that in the future drugs that effectively prevent ER-negative breast cancer will be used in combination with hormonal agents such as SERMs or aromatase inhibitors to prevent all forms of breast cancer.

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