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PI3K pathway inhibition in breast cancer

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Aberrant activation of the phosphatidylinositide 3-kinases (PI3K) pathway occurs frequently in breast cancer and contributes to treatment resistance. There has been a significant interest in developing inhibitors against components of the PI3K pathway, including PI3K, AKT and mTOR for the treatment of breast cancer. In estrogen receptor positive breast cancer, mutation in PIK3CA is the most common genetic abnormality in this tumor type and activation of the PI3K pathway has been associated with the development of acquired endocrine resistance. Everolimus, a mTOR inhibitor, has been shown to improve the efficacy of exemestane and is in clinical use for the treatment of non-steroidal aromatase inhibitor resistant estrogen receptor positive metastatic breast cancer. In triple negative breast cancer (TNBC), activation of the PI3K signaling has been attributed to the frequent loss of the negative regulators of this pathway, including PTEN and INPP4B. Laboratory and clinical trials are ongoing to establish PI3K pathway as a therapeutic target for TNBC. For HER2 positive breast cancer, inhibitors of PI3K pathway are being evaluated to overcome resistance to HER2 targeted agents. In this lecture, we will review genetic aberrations in components of this pathway in different subtypes of breast cancer, preclinical rational and the clinical development of inhibitors against this pathway.

Biography

Cynthia X. Ma obtained her M.D. in Beijing Medical University in China in 1990 and subsequently completed her Ph.D. at the University of Cincinnati in 1997 and Hematology and Oncology Fellowship from Mayo Clinic, Rochester in 2005. After graduation from her fellowship training, she was recruited by Washington University in St. Louis. She is currently an Associate Professor of Medicine and a Breast Oncologist at Washington University in St. Louis. She has published over 60 papers and is the Principal Investigator for multiple early phase clinical trials developing targeted therapeutics agents in breast cancer.

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