

5th World Congress on

BREAST CANCER

June 15-17, 2017 London, UK



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Endocrine treatment of breast cancer: Current concepts to predict and prevent relapse

Standard-of-care in endocrine treatment is the blockade of estrogen signaling via long-term estrogen deprivation. Tamoxifen, a selective ER modulator blocks 17 β -estradiol binding to stop tumor growth, and aromatase inhibitors (AI) block the aromatase enzyme to prevent conversion of androgens to estrogens. Despite their effectiveness one third of the patients develop recurrences leading to disease progression and death. Tamoxifen failure is attributed to a lack of bioactivation towards its active metabolite endoxifen that is mainly mediated by the polymorphic CYP2D6 enzyme for which distinct genetically determined functional variants are present in the general population. Inter-individual differences in CYP2D6 enzyme activities are grouped into the phenotypes ultra-rapid (UM), extensive (EM), intermediate (IM) and poor (PM) metabolizers. EM patients have high levels of endoxifen and are likely to benefit whereas PM patients have low endoxifen levels and a significant risk to relapse. Therefore, CYP2D6 polymorphism and plasma endoxifen levels may serve as tamoxifen outcome predictors however findings from others do not support this view. I will discuss the controversy and suggest a way forward towards the improvement of tamoxifen outcome. With regards to AI treatment, long-term estrogen deprivation leads to the reconfiguration of survival signaling in that reconfigured tumor cells eventually become sensitive towards estrogen, a mechanism known as E2-inducible apoptosis. While this is being explored in clinical trials I will show that distinct microRNA patterns characterize AI resistance and discuss their potential as biomarkers to identify patients at risk for relapse and those susceptible to E2-inducible apoptosis towards the prevention of relapse.

Biography

Hiltrud Brauch has completed her PhD at the University of Heidelberg, Germany, and Postdoctoral studies as a Fogarty International Visiting Fellow at the National Institutes of Health (NIH), National Cancer Institute (NCI) Frederick, Maryland, USA. She is the Deputy Director of Dr. Margarete Fischer-Bosch Institute of Clinical Pharmacology in Stuttgart, a non-profit private research institute of the Robert Bosch Foundation. She has published more than 250 papers in reputed journals and has been serving as an Editorial Board Member of pharmacogenetics and genomics as well as pharmacogenomics and personalized medicine.

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