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## PITX2 DNA-methylation, a novel validated predictive marker in high-risk breast cancer patients to assess the benefit of anthracycline based chemotherapy

Olaf G Wilhelm<sup>1</sup>, Manfred Schmitt<sup>1,2</sup>, Rudolf Napieralski<sup>1,2</sup>, Gabriele Schricker<sup>1</sup>, Wilko Weichert<sup>2</sup>, Aurelia Noske<sup>2</sup>, Jürgen Lauber<sup>3</sup>, Jonathan Perkins<sup>4</sup> and Marion Kiechle<sup>2</sup>

<sup>1</sup>Therawis Diagnostics, Germany

<sup>2</sup>Technical University of Munich, Germany

<sup>3</sup>QIAGEN, Germany

<sup>4</sup>Qiagen Ltd., Manchester, UK

**Background:** The term epigenetics describes dynamic alterations in a cell that switch genes on and off without changes in the DNA sequence. Examples of mechanisms that produce such changes are histone modification and DNA-methylation, each of which alters gene expression. A variety of cellular processes are influenced by epigenetic changes, including gene expression, cellular differentiation, genomic imprinting and embryogenesis; DNA-methylation plays a crucial role in the development of a variety of cancers, including breast cancer. Significant evidence has accumulated that methylation of the *PITX2* (paired-like homeodomain transcription factor 2) gene, an epigenetic event, might serve as a novel predictive and prognostic biomarker in high-risk breast cancer patients. (Inter) national guidelines recommend anthracycline-based chemotherapy for high-risk breast cancer patients as the standard-of-care, but not all patients do equally benefit from such a chemotherapy.

**Materials & Methodology:** The novel thesacscreen® *PITX2* RGQ PCR assay is a quantitative *in vitro* methylation specific real time PCR test (qMSP), intended for the determination of the percent methylation ratio (PMR) in the *PITX2* promoter 2 expressed by primary breast cancer tumor tissue (FFPE-material). After bisulfite exposure of extracted DNA to distinguish between methylated and unmethylated *PITX2* DNA, the percent methylation ratio (PMR) of the *PITX2* gene promoter 2 is quantified by qMSP. The PMR obtained does provide information to the treating physician about whether a patient is likely to respond to anthracycline-based chemotherapy.

**Results & Conclusions:** Data will be presented for 205 high-risk lymph node-positive, estrogen receptor-positive, HER2-negative breast cancer patients, treated with adjuvant anthracycline-based chemotherapy. The *PITX2* pre-defined cut-off value of PMR=12 demonstrated a statistically significant differentiation between low- and high-risk breast cancer patient for the primary endpoint DFS, also for patients treated with endocrine therapy in addition to anthracycline-based adjuvant therapy. High-risk lymph node-positive, estrogen-receptor-positive, HER2-negative breast cancer patients, with *PITX2* methylation defined as low (PMR≤12), are sufficiently treated with anthracycline-based chemotherapy, irrespective if treated with additional tamoxifen. High-risk lymph node-positive, estrogen receptor-positive, HER2-negative breast cancer patients with *PITX2* methylation defined as high (PMR>12) should avoid anthracycline-based chemotherapy. These patients are recommended to switch to other chemotherapy regimens, since with this *PITX2*-characteristics, the patient has a lower probability to respond to anthracycline-based chemotherapy.

### Biography

Olaf G Wilhelm is the Founder and Chief Executive Officer of Therawis Pharma GmbH, Munich. He was also the Co-Founder of Wilex Biotechnology GmbH and its Managing Director from October 1 1997 until April 8 2001 and has been Chief Executive Officer of WILEX AG since April 9 2001 (Willex AG). He managed two company acquisitions, several international development and commercialization partnerships and listed Willex AG on the public stock exchange. He received his MD from the Technical University of Munich (TUM) and was appointed Extraordinary Professor of Gynecology at the TUM in 2001. From 1990 to 1997, he was employed as Senior Physician for Obstetrics and Gynecological Oncology at the Department of Obstetrics & Gynecology (Frauenklinik) at the Medical School of the University Hospital Klinikum rechts der Isar at the TUM. While at the Technical University of Munich, he was also a member of the Clinical Research Unit of the Frauenklinik. From 1987 to 1990, he worked as a Scientist for Eli Lilly and Company, Indianapolis, Indiana/USA. He received the Midwest Trainee Award of the American Federation for Clinical Research and has authored over 70 publications. In 2011, the Technical University of Munich awarded him the title TUM Entrepreneur of Excellence.

barbara.fall@therawis.com