sysmex | Together for a better healthcare journey

PUBLICATION SPOTLIGHT

MammaTyper®

Comprehensive molecular subtyping of breast cancer patients – Clinical results

MammaTyper® is a molecular *in vitro* diagnostic test for precise, quantitative detection of the mRNA expression status of the genes HER2, ER, PR and Ki-67 in human breast cancer tissue. The combination of the four biomarkers enables the assessment of the different St. Gallen Breast Cancer molecular subtypes which provide prognostic information and are key parameters for treatment decisions in this cancer entity: Luminal A, Luminal B, HER2-positive and Triple-negative (Table 1).

MammaTyper® is an alternative approach to conventional immunohistochemistry (IHC) and hybridisation techniques, i.e. *in situ* hybridisation (ISH) and fluorescence *in situ* hybridisation (FISH), for the molecular subtyping of breast cancer patients with an invasive disease.

Table 1 *Definition of different breast cancer subtypes according to the St. Gallen classification.*

IHC subtype	Definition	Type of adjuvant therapy
Luminal A	HR+/HER2-/Ki-67-low	Endocrine therapy alone*
Luminal B	HR+/HER2-/Ki-67-high	Endocrine therapy ± cytotoxic therapy
Luminal B	HR+/HER2+	Cytotoxics + anti-HER2 + hormonal therapy
HER2-positive	HR–/HER2+	Cytotoxics + anti-HER2 therapy
Triple-negative	HR–/HER2–	Cytotoxics therapy

** A few patients require cytotoxics (such as high nodal status or other indicator of risk).*
Abbreviations: ***HR –*** *hormone receptor;* ***HER2 –*** *human epidermal growth factor receptor 2*

Several studies have shown a high concordance rate between MammaTyper® and IHC (Table 2), and recent results have demonstrated that MammaTyper® is a valuable alternative to IHC/FISH for discriminating the HER2-low subtype due to its higher accuracy in the detection of HER2 expression [2]. The excellent performance was confirmed in the study by Liu *et al.* [1] in which MammaTyper® was able to accurately stratify patients into prognostic groups based on their HER2 status. Especially nowadays, an accurate assessment of the HER2 status is of utmost importance, with the latest drugs being approved for this population.

MammaTyper® meets the need for standardised, quantitative and fast molecular subtyping enabling confident treatment.

Table 2 *Concordance of MammaTyper® versus immunohistochemistry deriving from several clinical studies.*

		Concordance MammaTyper® *versus* immunohistochemistry (%)			
References	**# Samples**	**HER2**	**PR**	**ER**	**Ki-67**
Wallwiener (2014)	28	100	81.5	81.9	n.a.
Deutsch (2015)	27	n.a.	85.2	70.4	50.0
Wirtz (2015)	9	88.9	88.9	88.9	44.5
Wirtz (2015)	719 (HER2), 719 (PR), 719 (ER), 688 (Ki-67)	91.8	82.5	91.8	75.0
Sinn (2017)	54	n.a.	92.9	91.2	n.a.
Stefanovic (2017)	67 (primary tumor)	100	70.0	81.0	n.a.
Stefanovic (2017)	67 (metastatic site)	89.0	78.0	84.0	n.a.
Fasching (2018)	418	84.9	82.4	91.5	n.a.
Teng (2018)	174 (HER2), 236 (PR), 240 (ER), 212 (Ki-67)	99.4	91.1	95.4	90.1
Saracchini (2019)	72 (HER2), 76 (PR), 76 (ER), 76 (Ki-67)	93.0	76.3	92.1	92.1
Hipfel (2019)	1.641 (HER2), 1.568 (PR), 1.628 (ER), 1.586 (Ki-67)	92.8	86.9	92.9	77.4
Shaaban (2020)	126 (HER2), 132 (PR), 132 (ER), 47 (Ki-67)	95.0	89.4	95.5	87.2
Median in %		**92.9**	**83.9**	**91.4**	**77.4**

Abbreviations: ***HER2 –*** *human epidermal growth factor receptor 2;* ***ER –*** *estrogen receptor;* ***PR –*** *progesterone receptor,* ***Ki-67 –*** *marker of proliferation,* ***n.a. –*** *not available*

www.sysmex-europe.com/MammaTyper

Comprehensive molecular subtyping of breast cancer patients – Clinical results

Selected publications

[1] Liu Y et al. (2023): *ERBB2 mRNA expression can better distinguish HER2-low/neg breast cancer prognosis. Abstract (569) ASCO.*

Key message: *MammaTyper® qRT-PCR assay may better reflect the prognosis of HER2-neg/low compared to IHC/FISH which could become interesting for the application of HER2-low targeted drugs.*

[2] Teng X et al. (2022): *ERBB2 mRNA Expression in HER2-low Breast Cancer. Poster (PB-101) OPTIMAL DIAGNOSIS.*

Key message: *Compared with IHC/FISH, MammaTyper® represents an alternative for distinguishing the HER2-low subtype in breast cancer by accurate detection of HER2 expression.*

[3] Shaaban AM et al. (2022): *Comparison of ER, PR, HER2 and Ki67 expression by MammaTyper® RT-qPCR and immunohistochemistry (IHC) on needle core biopsies of breast cancer. Poster (PB-087, abstract 263) OPTIMAL DIAGNOSIS.*

Key message: *MammaTyper® for molecular subtyping on needle biopsies represents a reliable, efficient and reproducible alternative for breast cancer 4-marker IHC analysis.*

[4] Caselli E et al. (2021): *Looking for more reliable biomarkers in breast cancer: Comparison between routine methods and RT-qPCR. PLoS One 16 (9): 1–18.*

Key message: *MammaTyper® to offer more precise assessment of endocrine responsiveness, improve Ki67 standardisation and help resolve equivocal HER2 IHC/FISH cases, leading to potential redistributions of the molecular subtypes.*

[5] Finsterbusch K et al. (2020): *Luminal A versus luminal B breast cancer: MammaTyper® mRNA versus immunohistochemical subtyping with an emphasis on standardised Ki67 labelling-based or mitotic activity index-based proliferation assessment. Histopathology 76 (5): 650–660.*

Key message: *High rates of agreement between MammaTyper® and IHC-based intrinsic subtyping of luminal HER2-negative breast cancer is feasible where the extent of the agreement depends on the applied proliferation assessment method.*

[6] Laible M et al. (2019): *Impact of molecular subtypes on the prediction of distant recurrence in estrogen receptor (ER) positive, human epidermal growth factor receptor 2 (HER2) negative breast cancer upon five years of endocrine therapy. BMC Cancer 19 (1): 1–9.*

Key message: *St. Gallen Luminal A-like tumours identified by MammaTyper® show markedly low rates of distant recurrence at 10 years of follow-up meaning that these patients could be omitted for chemotherapy.*

[7] Fasching PA et al. (2018): *Evaluation of the MammaTyper® as a molecular predictor for pathological complete response (pCR) after neoadjuvant chemotherapy (NACT) and outcome in patients with different breast cancer (BC) subtypes. Poster (227P) ESMO.*

Key message: *Standardised measurement of the 4 biomarker mRNAs by MammaTyper® is comparable to the determination of IHC level and is strongly associated with response to NACT based on a pre-treatment biopsy as well as long-term outcome.*

[8] Varga Z et al. (2017): *An international reproducibility study validating quantitative determination of ERBB2, ESR1, PGR, and MKI67 mRNA in breast cancer using MammaTyper®. Breast Cancer Research 19 (55): 1–13.*

Key message: *A prospective study in 10 international pathology labs has shown that MammaTyper® has potential to substantially improve the current standards of BC diagnostics by providing a highly precise and reproducible quantitative assessment of the 4 established BC biomarkers and molecular subtypes in a decentralised workup.*

[9] Wirtz RM et al. (2016): *Biological subtyping of early breast cancer: a study comparing RT-qPCR with immunohistochemistry. Breast Cancer Res Treat 157 (3): 437–446.*

Key message: *Concordance between MammaTyper® and IHC/CISH-based biomarker assessments was high (HER2 91.8%, ER 91.8%, PR 82.5%, Ki67 75.0%), while tumour Ki67 mRNA content was associated with DFS and OS of the FinHer trial patient cohort.*

[10] Laible M et al. (2016): *Technical validation of an RT-qPCR in vitro diagnostic test system for the determination of breast cancer molecular subtypes by quantification of ERBB2, ESR1, PGR and MKI67 mRNA levels from formalinfixed paraffin-embedded breast tumor specimens. BMC Cancer 16 (398): 1–14.*

Key message: *Based on a validation of the analytical performance, including site-to-site reproducibility of the individual marker analysis, MammaTyper® was judged to be a technical improvement to current standards for decentralised FFPE-based routine assessment of the 4 BC biomarkers to enable molecular subtyping.*

Last update August 2023

Distributor EMEA: Sysmex Europe GmbH · www.sysmex-europe.com
Manufacturer: Cerca Biotech · www.cercabiotech.com
You will find your local Sysmex representative's address under www.sysmex-europe.com/contacts

72002747 8.EN.N.08/23