Improving HER2 Status Assessment in Breast Cancer with MammaTyper®: Focus on Equivocal Cases

A. Velasco, PhD[1,2]; I. Urdanibia, PhD[1]; G. Rodríguez, MD[2]; N. Tuset, MD[2]; A. Gasol, MD[2] and S. Morales, MD, PhD[1,2]
[1]IRB LLEIDA, [2]HUAV LLEIDA; SPAIN

1026
PS4-04-02

1026
PS4-04-02

Abstract

Accurate HER2 status assessment is crucial for guiding treatment decisions in breast cancer.

MammaTyper® is a CE-marked in-vitro diagnostic resource utilizing real-time quantitative PCR (qRT-PCR) to quantify mRNA transcripts of ERBB2, ESR1, PGR, and MKI67. It provides an objective and standardized classification of breast cancer into intrinsic subtypes (Luminal A, Luminal B, HER2-enriched, and Triple-Negative), offering prognostic and predictive information that complements traditional immunohistochemistry (IHC).

MammaTyper®'s high reproducibility and sensitivity are particularly valuable when subjective interpretation of IHC presents challenges.

Introduction

The molecular classification of breast cancer plays a pivotal role in guiding personalized treatment strategies.

Traditionally, this classification is based on immunohistochemical (IHC) analysis of hormone receptors (estrogen and progesterone), the Ki67 proliferation index, and HER2 protein expression.

However, MammaTyper® represents a significant advancement in molecular profiling by utilizing quantitative reverse transcription PCR (RT-qPCR) to measure the messenger RNA (mRNA) levels of the corresponding genes.

This innovative approach offers superior precision and reproducibility, enabling more accurate molecular subtyping and, ultimately, more tailored therapeutic decisions for patients.

Objectives

This study aimed to analyze whether the MammaTyper® platform improves the classification of HER2-equivocal breast cancer cases and to assess its concordance with FISH-based methods.

Methods and Materials

We analyzed 93 breast cancer patients. Estrogen receptor (ER) and progesterone receptor (PR) status, along with Ki67 index, were determined by IHC. HER2 status was initially assessed by IHC and FISH (table 1). MammaTyper® was then performed to classify intrinsic subtypes and determine HER2 status based on *ERBB2* mRNA levels. Concordance between MammaTyper®, IHC, and FISH was evaluated (table2).

Results

MammaTyper® **confirms** HER2-positivity in 60% of the cases initially identified as positive by IHC/FISH (table 3).

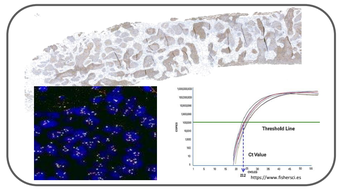
MammaTyper® identified a lower proportion of HER2-positive tumors (**34%**) compared to IHC alone (**45%**), showing **72% concordance** overall. This concordance was higher (**84%**) in HER2-negative tumors (table 4).

Discussion

MammaTyper®-positive cases showed a strong association with the FISH ratio though a significant finding is that 31% of the cases MammaTyper® called **HER2-negative** still had a high FISH ratio (> 2), suggesting potential disagreement on the true *biological* status or technical limitations (table 5).

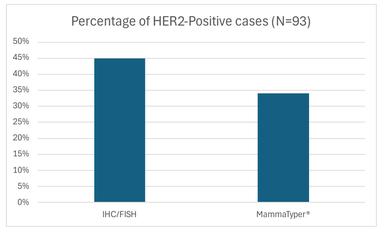
Marker (IHC)	Positive Cases (N=93)	% Percentage
Estrogen Receptor (ER)	83	89%
Progesterone Receptor (PR)	42	45%
Ki67 Index (High)	51	55%

Table 1. Status of the primary tumor markers (ER, PR, and Ki67) assessed by Immunohistochemistry (IHC) across the entire patient cohort.



MammaTyper® Classification	Total Cases	Cases with High FISH Ratio (≥2)	% Percentage of Group
HER2-Positive	32	23	71%
HER2-Negative	55	17	31%

Table 5. MammaTyper® vs. HER2 FISH Ratio

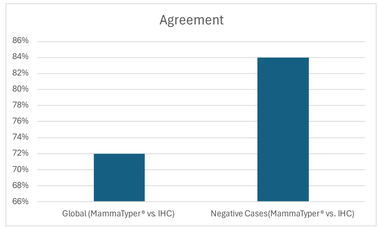


Total Cases	93
Overall Concordance	0,73
Concordance in IHC/FISH-Positive Cases	0,6
Concordance in IHC/FISH-Negative Cases	0,84

Table 2. Overall agreement (concordance) between the IHC/FISH combined assessment and the MammaTyper® assay for HER2 status.

Concordance Metric	% Value
Overall Concordance (MammaTyper® vs. IHC)	72%
Concordance in IHC-Negative Cases	84%
Proportion of HER2-Positive Tumors by MammaT	34%
Proportion of HER2-Positive Tumors by IHC	45%

Table 4. MammaTyper® vs. IHC (Single Marker)



IHC/FISH Classification	Total Cases	MammaTyper® Result	Cases Positive by MammaTyper®	Percentage of Group
HER2-Positive	42	Confirmed Positive	25	60%
HER2-Negative	51	Misclassified Positive	8	15%
Total HER2-Positive by MammaTyper®			32	34% of all 93 cases
Total HER2-Positive by IHC/FISH			42	45% of all 93 cases

Table 3. MammaTyper® vs. IHC/FISH for HER2 Status

Conclusions

MammaTyper® demonstrates substantial concordance with IHC and FISH for HER2 status determination, particularly in HER2-negative cases. It identifies a smaller subset of HER2-positive tumors compared to IHC, suggesting its potential to refine the selection of patients for HER2-targeted therapies. Further clinical utility should be assessed by correlating MammaTyper® results with treatment response and survival outcomes.

Contact

Ana Velasco Sanchez, Biologist PhD
Institut de Recerca Biomèdica de Lleida – Fundació Dr. Pifarré, IRBLleida (ROR: 03mfyme49)
Email: avelasco@irblleida.cat
Website: https://www.irblleida.org
Phone: +34973003749

References

1. Baez-Navarro X, Rigg J, Zylberberg D, van der Made A, Dubois D, Vanderveken J, Benhaddi N, Duhoux FP, Vernaeve H, Vassilieff M, Berlière M, Galant C, van Deurzen CHM, van Bockstal MR. Reproducibility of Equivocal HER2 In Situ Hybridization Groups 3 and 4, and Comparison With HER2 mRNA Expression: The Thin Line Between Amplified and Nonamplified Breast Cancers. Arch Pathol Lab Med. 2025 Apr 28. doi: 10.5858/arpa.2024-0499-OA. Epub ahead of print. PMID: 40289717.
2. Baez-Navarro X, van Bockstal MR, van der Made A, van Deurzen CHM. A Comparison Between Immunohistochemistry and mRNA Expression to Identify Human Epidermal Growth Factor Receptor 2-Low Breast Cancer. Arch Pathol Lab Med. 2025 Jul 1;149(7):635-642. doi: 10.5858/arpa.2024-0255-OA. PMID: 39471829.
3. Atallah N, Makhlouf S, Li X, Zhang Y, Mongan NP, Rakha E. Prediction of Response to Anti-HER2 Therapy Using A Multigene Assay. Mod Pathol. 2025 Apr;38(4):100713. doi: 10.1016/j.modpat.2025.100713. Epub 2025 Jan 16. Erratum in: Mod Pathol. 2025 Sep;38(9):100861. doi: 10.1016/j.modpat.2025.100861. PMID: 39826800.

This presentation is the intellectual property of the author/presenter. Contact them at avelasco@irblleida.cat for permission to reprint and/or distribute.

© POSTER TEMPLATE BY GENIGRAPHICS® 1.800.790.4001 WWW.GENIGRAPHICS.COM