

Clinical significance of immunohistochemistry in breast cancer diagnostics

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentlig försvaras i Arvid Carlsson, Medicinargatan 3, fredagen den 26 Maj 2023, klockan 09.00.

av Slavica Janeva

Fakultetsopponent:
Professor Jonas Manjer
Lunds Universitet, Sverige

Avhandlingen baseras på följande delarbeten

- I. **Janeva S**, Parris TZ, Nasic S, De Lara S, Larsson K, Audisio RA, Olofsson Bagge R, Kovács A. Comparison of breast cancer surrogate subtyping using a closed-system RT-qPCR breast cancer assay and immunohistochemistry on 100 core needle biopsies with matching surgical specimens. *BMC Cancer* 2021 Apr 21;21(1):439.
- II. **Janeva S**, Krabbe E, Parris TZ, Nasic, S, Sundquist M, Karlsson P, Audisio RA, Olofsson Bagge R, Kovács A. Clinical evaluation of molecular surrogate subtypes in patients with ipsilateral multifocal primary breast cancer. *Breast Cancer Research* 2023 Apr 6;25(1):36.
- III. **Janeva S**, Parris TZ, Krabbe E, Sundquist M, Karlsson P, Audisio RA, Olofsson Bagge R, Kovács A. Clinical relevance of biomarker discordance between primary breast cancers and synchronous axillary lymph node metastases. *Submitted, under revision*
- IV. **Janeva S**, Zhang C, Kovács A, Parris TZ, Crozier JA, Pezzi CM, Linderholm B, Audisio RA, Olofsson Bagge R. Adjuvant chemotherapy and survival in women aged 70 years and older with triple-negative breast cancer: a Swedish population-based propensity score-matched analysis. *Lancet Healthy Longevity* 2020 Dec;1(3):e117-e124.

**SAHLGRENKA AKADEMIN
INSTITUTIONEN FÖR BIOMEDICIN**



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Abstract

For patients with breast cancer, modern patient-tailored treatment depends on tumor-specific characteristics, i.e., estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor 2 (HER2), and the proliferation marker Ki67. These biomarkers are used in different combinations to classify breast cancer into subtypes on which treatment recommendations are based. Although modern multi-gene tests are available, the cornerstone for assessing these biomarkers remains immunohistochemistry (IHC). This thesis is aimed at investigating various clinical aspects of IHC and breast cancer subtypes in breast cancer diagnostics and treatment.

In Paper I, the mRNA-based assessment tool STRAT4 was compared with IHC, and the potential changes in adjuvant treatment recommendations based on the differences between tests were compared. The results indicated that adjuvant treatment decisions based on STRAT4 rather than IHC were more aggressive.

Paper II investigated whether IHC assessment on more foci than only the largest focus in patients with multifocal breast cancer would affect adjuvant treatment recommendations. The results suggest that all detected foci within a breast specimen should be assessed with IHC.

Because guidelines do not recommend IHC assessment of lymph node metastasis (LNM), Paper III investigated whether treatment recommendations might differ if the biomarker status in the LNMs were known. Although both biomarker and subtype discordance was observed, no additional treatment was recommended according to these changes.

Paper IV, a national population-based registry study, investigated the effects of chemotherapy on survival outcomes in women ≥ 70 years of age with a breast cancer subtype lacking ER, PR, and HER2 biomarker expression, i.e., those with triple-negative breast cancer. Statistically significant survival benefits were shown for women treated with adjuvant chemotherapy, thus highlighting the importance of considering chemotherapy in this group of older patients.

Key words: breast cancer biomarkers, immunohistochemistry, surrogate subtype, RT-qPCR, multifocal breast cancer, lymph node metastasis, triple-negative breast cancer, older women

ISBN: 978-91-8069-267-0 (TRYCK)

<http://hdl.handle.net/2077/75206>

ISBN: 978-91-8069-268-7 (PDF)