PhD Thesis – Half Time Review
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Prognostic and Monitoring Factors in Invasive Lobular Carcinoma of the Breast

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Abstract

**Background:** Invasive lobular carcinoma (ILC) comprises approximately 10% of all breast cancer. ILC has, compared to other histological subtypes, a variety of distinguishing features. Nevertheless, current treatments are similar. Studies on ILC are limited and sample sizes often small.

**Aim:** The overall aim of this project is to evaluate the clinical value of prognostic and monitoring factors in different subsets of primary and metastatic ILC.

**Methods:** *Paper I:* Well-established prognostic factors, with a special focus on Ki67 and Nottingham histological grade (NHG) were analyzed in a retrospective ILC cohort of well-characterised patients (N=192) with long term follow-up (median 21-years). Furthermore, Ki67, NHG and estrogen receptor (ER) together with tumor size (T) and nodal status (N) were combined into a prognostic index (KiGE-TN). Primary endpoint was breast cancer mortality (BCM). *Paper II:* The study is based on an extended version of the cohort in Paper I, including exclusively ER-positive/HER2-negative ILC (N=225). New putative prognostic biomarkers (amplified in breast cancer 1 (AIB1), androgen receptor (AR) and G protein-coupled estrogen receptor (GPER)), related to endocrine signaling pathways, were analyzed. Primary endpoint was BCM. Validating gene expression analysis of these biomarkers was also performed in publicly available ILC datasets.

**Further studies:** *Paper III:* Is the current surgical management of the axilla, based on the ACOSOG Z0011 study, still applicable in ILC? The relationship between non-sentinel lymph node metastases in ILC vs. invasive carcinoma of no special type (NST) in patients with 1-2 metastases in sentinel node biopsy, will be investigated. *Paper IV:* Circulating tumor cells, diagnostic imaging and tumor marker CA 15-3 as monitoring factors for disease progression in metastatic ILC (N=28) vs. NST, will be evaluated in a prospective observational cohort.

**Results:** *Paper I:* Ki67 and NHG were independent prognostic factors significantly associated with BCM, and KiGE-TN could identify a low-risk group with an excellent long-term prognosis. *Paper II:* AIB1 was an independent prognostic factor for BCM and the result was strengthened by validating gene expression analyses. AR and GPER showed no prognostic effects.

**Conclusions:** Well-established prognostic factors seem to be valid, and AIB1 is a new putative prognostic biomarker, in ILC.

*Paper I:* Published

*Paper II:* Submitted to Breast Cancer Research and Treatment Oct-21-2018