Aspects of endocrine therapy in primary breast cancer

Ph.D Thesis
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ABSTRACT

BACKGROUND
Oestrogen receptor positive (ER+), human epidermal receptor 2 negative (HER2-) breast cancers are classified as Luminal A or B based on gene expression, but immunohistochemical (IHC) markers are used in clinic for surrogate subtyping for adjuvant treatment decision; endocrine or additional chemotherapy. Additional biomarkers are needed to better forecast prognosis and prediction of therapy.

AIMS
I. Examine adherence to adjuvant endocrine therapy after 3 and 5 years, respectively.

II. Examine the agreement between molecular subtyping (MS) and surrogate subtyping.

III. The effect of molecular profiles for prognosis and prediction of tamoxifen benefit after 30 years of follow-up in a premenopausal cohort.

IV. The prognostic and predictive impact of TILs (tumour infiltrating lymphocytes) in a premenopausal cohort with 30 years of follow-up and the impact of TILs on the first metastatic site.

STUDY COHORTS & METHODS

Project I: The Swedish National Quality Register for Breast Cancer was used to identify patients diagnosed with ER+ breast cancer. Adherence was based on data from the Swedish Prescribed Drug Register, defined as MPR (Medical Possession Ratio) ≥ 80%.

Project II: The study cohort consisted of patients with primary ER+/HER2- breast cancer from the SCAN-B project. Agreement (%) and kappa (κ) were used as concordance measures between MS and surrogate subtyping.

Project III + IV: Assessment of TILs and extraction of RNA for molecular profiling are performed from tumour tissues in the SBII:2pre study.

RESULTS
I. 91.2% and 91.5% were adherent after 3 and 5 years of treatment, respectively. No subgroups were significantly associated with adherence.

II. Agreement between MS and surrogate classifications was 62-70%. A combination of Ki67 and HG (histological grade) could identify 51% of the cohort with > 91% Luminal A tumours.

IMPLICATIONS
To tailor adjuvant treatment for patients with luminal tumors, more precise subtyping is necessary. Molecular assays are expensive and some patients might be spared genomic tests based on routine IHC. When de-escalating adjuvant treatment including only endocrine therapy, adherence is of importance to achieve satisfactory results. The ongoing studies will increase the knowledge of molecular profiling and TILs as a biomarker in premenopausal women for prognosis and prediction of adjuvant tamoxifen treatment.
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