

INTRODUCTION

The treatment of breast cancer in women and men is largely determined by the biology of the tumour. It is becoming more evident through this research that a patient's immunity can be an important indicator of what treatment is needed and how their own immune system can significantly contribute to their chances of long-term survival.

What are TILs? TILs are immune cells that are part of a person's biology. TILs are proving to be an important biomarker in cancer patients as they can play a part in killing tumour cells, particularly in some types of breast cancers. Identifying and measuring TILs can help to better target treatments particularly immunotherapy and may result in lower levels of other more aggressive treatments, including chemotherapy.

The importance of integrating biomarkers into the TNM staging has been emphasized in the 8th Edition of the American Joint Committee on Cancer (AJCC) Staging system. In a pooled analysis of 2148 TNBC-patients in the adjuvant setting, TILs are found to strongly up and downstage traditional pathological-staging in the Pathological and Clinical Prognostic Stage Groups from the AJCC 8th edition Cancer Staging System. This suggest that clinical and research studies on TNBC should take TILs into account in addition to stage, as for example patients with stage II TNBC and high TILs have a better outcome than patients with stage I and low TILs (1).

Furthermore, in a pooled analysis of phase 3 adjuvant and neo-adjuvant TNBC-trials, TILs predict outcome (2). TILs have therefore level-of-evidence IB as a prognostic factor.

In addition, Park et al., demonstrated in a pooled analysis of untreated TNBC-patients that patients with stage I TNBC and high TILs have 98% 5-year survival (3). Similar findings were found in young (<40 years) TNBC-patients that never received adjuvant systemic chemotherapy, with 15-years follow-up and with excellent outcome, and with a risk of recurrence of <2% (4).

In the KN119-study, (NCT02555657) that was a randomized, open-label, phase 3 study of pembrolizumab monotherapy versus investigator's choice of single-agent chemotherapy in patients with previously treated metastatic TNBC, TILs were significantly associated with better clinical outcomes with pembrolizumab monotherapy but not single-agent chemotherapy (5). In the biomarker-analysis of Impassion130 (NCT02425891), TILs predicted benefit to PDL1-inhibition with atezolizumab, for any PDL1-stain (6). Both phase 3-studies suggest that TILs can be an important predictive biomarker for immunotherapy, as a complement to PDL1.

Given its increasing importance in the use of TILs in breast cancer daily clinical practice, its potential use in clinical trials as well as its potential importance for industry and patients, needs to be investigated more in detail, and this includes machine learning approaches to TILs.

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