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Editorial

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Therapeutic Strategies in Triple-Negative Breast Cancer

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Triple-negative breast cancer (TNBC) represents one of the most studied recent research topics with more than 1,500 papers published in 2016. This breast cancer subtype comprises 15–20% of all breast cancer cases and is characterized by aggressive clinical characteristics and a particularly poor outcome [1]. Compared to estrogen receptor (ER)-positive cancers, TNBC carries an increased 5-year relapse risk, an increased probability for visceral involvement, but at the same time a decreased risk for bone metastases. TNBC is more likely to occur in younger women, *BRCA1* germline mutation carriers, and African Americans.

In recent years, it has been recognized that TNBC is characterized by significant heterogeneity and what used to be viewed as one single breast cancer entity is now differentiated into a number of sub-types, based on genetic profiles and distinct tumor biological features. The resulting therapeutic consequences are exemplified by differing chemotherapeutic sensitivity observed for some subtypes and by the need for individualized therapy. This heterogeneity establishes the need for identifying molecular markers that may help refine therapeutic management within the overall class of TNBC disease. In their review Michael Hubalek and colleagues [2] discuss the molecular subtypes that comprise promising predictive molecular markers for tailoring therapy in the – until recently – ill-characterized entity of TNBC. He also reviews possible therapeutic strategies that arise from our improved knowledge of the particular biological behavior of tumors classified into a particular subgroup.

Since TNBC is the dominant subtype in *BRCA1* carriers, and because of the therapeutic consequences that are associated with BRCA deficiency, genetic testing is increasingly recommended for all women with TNBC younger than 60 years. The presence of *BRCA* germline mutations not only impacts local treatment strategies, but also increasingly guides systemic therapy and prophylactic surgery. The article by Eric Hahnen and colleagues [3] sheds light on the often underrated prevalence of *BRCA1* mutations in TNBC and reviews testing strategies, guidelines, and clinical consequences that have become standards of care in this distinct patient population.

Mutational processes that drive the inter- and intra-tumor heterogeneity in TNBC have been the subject of several recent reviews, but in particular it has been shown that TNBC is composed of at least 4–6 definable molecular subtypes and multiple distinct oncogenic signaling pathways [4]. Whether chemotherapy choices should be different among TNBC subtypes is now being debated, considering that chemotherapy, the mainstay of treatment generally involving anthracyclines, taxanes, and/or platinum compounds, is of clearly limited efficacy [1]. Among the altered signaling pathways, the DNA damage repair pathway has been reported to be of particular relevance. It is mainly characterized by altered *BRCA* gene functionality, but MAP kinases and PIK3 kinases also seem to play a relevant role in this game [5].

In this issue of Breast Care Andreopoulou and colleagues [6] have put forward a comprehensive review on the established cytotoxic and emerging targeted therapies for TNBC. It becomes increasingly evident that new procedures are addressing different targets and innovative conceptual approaches. Among the most interesting concepts, the authors review new trials looking at the utilization of 'old' drugs (platinum-derived compounds, taxanes, anti-tubulins) in better selected TNBC subgroups, the DNA repair pathways (BRCA or BRCA-like tumors) as the target of several anti-PARP drugs now in advanced experimental clinical phase, the possibility of modulation of the immune status, targeting cancer-associated fibroblasts, angiogenic characteritstics, DNA plasticity, etc.

The improvement of outcome of this disease appears to be strictly related to the results that such therapies will bring in the near future in combination with 'old' cytotoxic approaches and/or utilized in different therapeutic regimens, such as neoadjuvant, maintenance, or preventive settings [7].

However, we remain convinced that clinically relevant results will be obtained only when we have powerful and precise validated biomarkers that enable us to better select patients to be treated and drugs to be utilized for the therapeutic strategy of this disease so difficult to approach.

Disclosure Statement

The authors declare that there are no conflicts of interest regarding this article.

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