Chairperson's Introduction

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Over recent years opportunities and need have both driven changes in the development and application of prognostic and predictive factors for the management of breast cancer. During the late 1980s and through much of the 1990s there was a near avalanche of reports on biomarkers in breast cancer tissues or less commonly in blood that were associated with prognosis. Virtually none of these translated into tests used in clinical practise because their use did not influence management. The reasons for this inapplicability included underpowered trials that could not be confirmed on repeat, insufficient discrimination of differing prognosis and the lack of change of clinical management merited by the variable prognosis. This led to what became something of a mantra for those interested in biomarkers: "I'm not interested in prognostic factors, I'm only interested in prediction". This could be seen in practice with, for example, the relative sparse testing for HER2, although it has prognostic significance, until such time as the need to use its predictive value for directing trastuzumab therapy became apparent.

While the need for predictive markers remains there is now wide acceptance of the value of some prognostic markers that may identify women at such good risk that they need no further treatment after surgery or in addition to endocrine therapy for ER+ patients. Indeed, in a web-based survey of breast cancer professionals conducted in 2006/07 this topic won 50% more support as the most important translational research question in breast cancer than any other. This importance has been driven by the very good prognosis of much breast cancer diagnosed over recent years, particularly that of screen-detected disease and the substantial effects of modern endocrine therapy making chemotherapy in many of the patients inappropriate. As well as conventional investigation of single biomarkers or small combinations of them, use of genome screening studies has generated RNA-based multi-gene prognostic predictors such as the OncotypeDx and Mammoprint whose impact on clinical management is now being studied in large prospective clinical trials.

The identification of predictive factors in breast cancer as in other disease types focuses around the targets of therapy and has yielded the two archetypical markers, ER and HER2. The plethora of new, targeted therapies has been expected to yield multiple new predictive markers based around the target but this has been complicated by the need to identify critical components or features of a targeted pathway rather than simple presence or absence of a target.

There is great optimism that the substantive research efforts in this area will yield early substantial advances to allow the extension of personalised medicine. The potential for this is clear to see and makes the application of a clear understanding of the requirements for taking a hopeful candidate marker to a usable clinical tool more important than ever. The goals of this educational chapter are therefore to provide a better understanding of some of these rules starting from the distinction of prognosis and prediction, extending through the application of the rules to multigene predictors and finishing with a consideration of what evidence is needed to allow the clinician to introduce a new marker or profile into his or her routine practice.

Conflict of interest statement

None declared.