Examination of "Her2 Low" patient populations for prediction to Her2-targeting antibody-drug conjugate response in Her2 negative patients using a novel high sensitivity immunohistochemistry assay

Joseph Krueger, Kenneth Bloom, George Abel, Hisatoaki Okada, Hiroaki Yotaka
Invicro, a Konica Minolta Company, Boston, MA & Konica Minolta Precision Medicine, Japan

Abstract

The positive results for trastuzumab deruxtecan (DS-8201) in Her2+ breast cancer from the pivotal phase III DESTINY-Breast01 trial announced in late 2019 represent a pivotal change in the approach to anti-Her2 therapy. Specifically, an antibody-drug conjugate (ADC) utilizes an extracellular domain (ECD) that targets T-lymphocytes and is thought to have a key benefit in mechanisms of action over a more classic anti-Her2, trastuzumab (Herceptin), or other intracellular-enterosome based immunotherapies. However, determining the efficacy of such a new class of ADCs in clinical practice still remains challenging in clinical practice after nearly 15 years of improvements in scoring interpretations led by ASCO/CAP. The demand for improved testing performance is unlikely to be met through changing Her2 IHC interpretation, as the existing Her2 companion diagnostic strategy has the ability to classify "Her2 Low" patients into the standard 0+/1+/2+/3+ classes. The Quanticell approach creates the potential to develop a new patient classification that can be used to predict patient response for these therapies. Based on clinical data being presented from novel anti-Her2 therapies, such as DS-8201, which have efficacy in "Her2 negative" patients, it may be necessary to redefine patient classes from the current Her2 "high"/"low" paradigm.

Methods

A breast tumor tissue microarray (TMA) was stained with standard immunohistochemistry (IHC) to predict response. In comparison to DAB, the Quanticell approach resulted in much higher dynamic range, allowing clearer detection and precise quantification of Her2 across all patient samples regardless of the range of Her2 expression.

Discussion

Based on clinical data being presented from novel anti-Her2 therapies, such as DS-8201, which show efficacy in "Her2 negative" patients, it may be necessary to redefine patient classes from the classical Her2 "positive" or "negative" assignments and include a novel "Her2 Low" classification. Based on the available clinical studies, the existing DAB IHC approach is not able to correctly identify a "Her2 Low" classification. Therefore, we introduce the Quanticell IHC method as an approach which may enable ideal patient stratification for the novel anti-Her2 ADC therapies by creating new classes of "Her2 Low" and "Her2 positive" which can be used to predict patient response for these therapeutics.