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EGFR expression is associated with decreased benefit from trastuzumab in the NCCTG N9831 (Alliance) trial.

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Abstract

BACKGROUND:

Epidermal growth factor receptor (EGFR) has been hypothesised to modulate the effectiveness of anti-HER2 therapy. We used a standardised, quantitative immunofluorescence assay and a novel EGFR antibody to evaluate the correlation between EGFR expression and clinical outcome in the North Central Cancer Treatment Group (NCCTG) N9831 trial.

METHODS:

Tissue microarrays were constructed that allowed analysis of 1365 patients randomly assigned to receive chemotherapy alone (Arm A), sequential trastuzumab after chemotherapy (Arm B) and chemotherapy with concurrent trastuzumab (Arm C). Measurement of EGFR was performed using the EGFR antibody, D38B1, on the fluorescence-based AQUA platform. The result was validated using an independent retrospective metastatic breast cancer cohort (n=130).

RESULTS:

Epidermal growth factor receptor assessed as a continuous (logarithmic transformed) variable shows an association with disease-free survival in Arm C (P=0.009) but not in Arm A or B. High EGFR expression was associated with worse outcome (Hazard ratio (HR)=2.15; 95% CI 1.28-3.60, P=0.004). Validation in a Greek metastatic breast cancer cohort showed an HR associated with high EGFR expression of 1.92 (P=0.0073).

CONCLUSIONS:

High expression of EGFR appears to be associated with decreased benefit from adjuvant concurrent trastuzumab. Since other treatment options exist for HER2-driven tumours, further validation of these data may select patients for alternative or additive therapy.