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# Prognostic and predictive value of p-Akt, EGFR, and p-mTOR in early breast cancer.

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## Abstract

### BACKGROUND AND PURPOSE:

There are scarce data available on the prognostic/predictive value of p-Akt and p-mTOR protein expression in patients with high-risk early breast cancer.

### PATIENTS AND METHODS:

Formalin-fixed paraffin-embedded (FFPE) tumor tissue samples from 997 patients participating in two adjuvant phase III trials were assessed for EGFR, PTEN, p-Akt, p-mTOR protein expression, and PIK3CA mutational status. These markers were evaluated for associations with each other and with selected patient and tumor characteristics, immunohistochemical subtypes, disease-free survival (DFS), and overall survival (OS).

### RESULTS:

p-mTOR protein expression was negatively associated with EGFR and positively associated with PTEN, with p-Akt473, and with the presence of PIK3CA mutations. EGFR expression was positively associated with p-Akt473, p-Akt308, and PIK3CA wild-type tumors. Finally, p-Akt308 was positively associated with p-Akt473 expression. In univariate analysis, EGFR ($p = 0.016$) and the coexpression of EGFR and p-mTOR ($p = 0.015$) were associated with poor OS. Among patients with p-Akt308-negative or low-expressing tumors, those treated with hormonal therapy were associated with decreased risk for both relapse and death ($p = 0.013$ and $p < 0.001$, respectively). In the subgroup of patients with locoregional relapse, positive EGFR and mTOR protein expression was found to be associated with increased ($p = 0.034$) and decreased ($p < 0.001$) risk for earlier relapse, respectively. In multivariate analysis, low levels of p-Akt308 and the coexpression of EGFR and p-mTOR retained their prognostic value.

### CONCLUSION:

Low protein expression of p-Akt308 was associated with improved DFS and OS among patients treated with hormonal therapy following adjuvant chemotherapy. Coexpression of EGFR and p-mTOR was associated with worse OS.