Targeted therapy in triple-negative breast cancer: A case series

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Abstract

At least 20% of breast cancers are characterized by triple-negative receptor status (negative for estrogen receptor, progesterone receptor, and HER2). Human epidermal growth-factor receptor (EGFR) is a member of the EGFR/ErbB/HER family of Type I transmembrane tyrosine kinase receptors. Nine patients had TN-EGFR-positive with metastatic breast cancer (MBC). EGFR positivity was defined as staining in >10% of tumor cells by Immunohistochemistry. In total, nine patients were enrolled that the mean age was 46.7 years. All patients were from Kurdish ethnicity in west of Iran. Patients received erlotinib 150 mg daily. This suggests there may be a subset of TN, EGFR-positive MBC for whom EGFR-directed therapy may be suitable or that the natural history of their disease was indolent. Future studies to determine molecular and clinical profiles of patients likely to benefit from EGFR-tyrosine kinase inhibitor therapy.

Key words: Breast cancer, erlotinib, targeted therapy, triple negative

INTRODUCTION

In 2010, 209,060 patients were expected to be diagnosed with breast cancer in the United States.[¹] At least 20% of breast cancers are characterized by triple-negative receptor status (negative for estrogen receptor, progesterone receptor [PR], and HER2).[²] Triple-negative breast cancer (TNBC) is an aggressive histological subtype with limited treatment options and very poor prognosis following progression after standard chemotherapeutic regimen.[³] The cause of death of patients with TNBC is often a recurrence (30–40% of TNBC cases), which presents as distant metastasis.[⁴] Human epidermal growth-factor receptor (EGFR) is a member of the EGFR/ErbB/HER family of Type I transmembrane tyrosine kinase receptors. The ErbB receptors play an essential role in organ development and growth by regulating both the differentiation and morphology of cells and tissues. However, specific members most notably EGFR, are frequently overexpressed, and this aberrant expression and the signaling event it elicits induce erroneous development and unrestricted proliferation in a number of human malignancies including breast cancer.[⁵] Increased activation of EGFR and/or HER-2 will eventually result in uncontrolled proliferation, a hallmark of cancer cells. In addition, the cells harboring overexpressed EGFR, or improper regulation of EGFR activation may decrease apoptosis, increase metastasis and even angiogenesis. Dysfunctional EGFR-signaling networks are reportedly present in a cohort of breast carcinomas with poor prognosis.[⁵,⁶] We present 9 patients with metastatic breast cancer (MBC) that they had triple negative and EGFR positive.

METHODS

Nine patients had TN-EGFR-positive with MBC. EGFR positivity was defined as staining in >10% of tumor cells by immunohistochemistry. Patients required measurable disease, prior treatment with an anthracycline and taxane (adjuvant or metastatic setting). Patients
received erlotinib 150 mg daily. Primary endpoint was progression-free survival (PFS). Initially, nine patients were accrued.

**RESULTS**

In total, nine patients were enrolled that the mean age was 46.7 years. All patients were from Kurdish ethnicity in west of Iran. Drug can be tolerable for all of our patients with acceptable side effects. Six patients had prior chemotherapy for MBC. Three of patients had complaint with liver metastasis that not progress during the time of treatment. Four of them had bone metastasis that in three of them bone pain decrease significantly. Three patients progressed rapidly, and median PFS was 3 months for others. However, one patient had stable disease for 5 months. Treatment was well-tolerated. Toxicities in the six patients included grade 2 rash, grade 1 diarrhea.

The treatment of our patient’s erlotinib regimen resulted in antitumor activity in breast cancer in which an activated EGFR pathway was demonstrated. This finding is consistent with available preclinical and clinical data on EGFR tyrosine kinase inhibitors (TKIs) across tumor types and supports the efforts to optimize EGFR selective inhibitors in treating breast cancer and other malignancies.

**DISCUSSION**

Triple-negative breast cancer is defined by a lack of expression of estrogen and PR as well as human EGFR,[3] and TNBC comprises a heterogeneous subgroup of tumors including, but not limited to those classified as basal-like and claudin-low subtypes by expression profiling, and accounts for ~ 15% of all breast cancers.[4] Although TNBCs have higher response rates to neoadjuvant chemotherapy, TNBC patients show a higher rate of recurrence and poorer prognosis than other types of breast cancers.[5] Inhibitors of EGFR tyrosine kinases, such as erlotinib and gefitinib, have not been very effective in the treatment of breast cancer although many breast cancer cells express EGFR.[4,9,10] In our study, a number of TN patients with Kurdish ethnicity and treated with erlotinib had a successful treatment. TNBC largely represents a subtype of breast tumors with unique molecular and clinical characteristics, distinctive risk factors and patterns of recurrence, association with BRCA1 mutation status, inferior prognosis, and expanding therapeutic options. Multiple excellent approaches to improve care of TNBC, including DNA-damaging agents such as platinum, targeted agents against EGFR, vascular endothelial growth factor, and poly adenosine diphosphate ribose polymerase inhibitors are under investigation. Current research strategies are aimed at better understanding both the risk factors and the biology underlying TNBC, with the goal of developing preventive measures and improving treatment strategies for this challenging subtype of breast cancer.

Most patients progressed rapidly but in our study, six of nine patients had prolonged stable disease. This suggests there may be a subset of TN, EGFR-positive MBC for whom EGFR-directed therapy may be suitable or that the natural history of their disease was indolent. Future studies to determine molecular and clinical profiles of patients likely to benefit from EGFR-TKI therapy.

![Image](Image)

**REFERENCES**

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