bind to *HER2*, to *estrogen receptor*, or to *progesterone receptor*.

Triple-negative breast cancer cannot be treated with Herceptin or with antiestrogen drugs, since (by definition) the tumor cells do not contain the targets of these drugs (42). Hence, triple-negative breast cancer is treated with conventional small-molecule drugs. Triple-negative breast cancers overexpress human EGFR-1 (HER1). Although "HER1" has a name similar to "*HER2*," it is not the same protein. Because of this cancer's high expression of HER1, there has been some interest in treating triple-negative patients with cetuximab (Erbitux®), an antibody that binds to HER1 (43,44).

This introduces the function of *HER2*, and describes its relationship to other cell signaling proteins. HER2 is a membrane-bound protein that transmits signals, by way of a cell signaling pathway, to phosphatidylinositol-3,4,5-trisphosphate kinase (PI3K) (45,46). PI3K is in a class of enzymes called kinases. Kinases catalyze the phosphorylation of specific target molecules. Drugs that inhibit PI3 kinases are used for treating a variety of cancers (47). PI3 kinases, which catalyze the phosphorylation of certain lipids, regulate survival, proliferation, and apoptosis in normal cells as well as in cancer cells (48).

2. *Biomarkers in Breast Cancer—The Vogel Study*

Trastuzumab (Herceptin), an antibody that specifically binds to *HER2*, is used for treating breast cancer. In a study of 108 breast cancer patients, Vogel et al. (49) assessed the efficacy of trastuzumab, and attempted to find a correlation between expression of *HER2* in tumor biopsies with efficacy of the drug. Efficacy was measured by two endpoints, objective response and time to progression (TTP).

According to the endpoint of objective response, efficacy was found in 34% of patients who *overexpressed HER2*, but only in 7% in patients bearing tumors with *normal expression of HER2*. These measures of objective response represent the sum of data on complete response and partial response. Partial response was defined by a greater than 50% decrease in the sum of the products of the perpendicular diameters of all measurable lesions.

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