

ABSTRACT FORM

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TRASTUZUMAB AS AN ADJUVANT TREATMENT FOR EARLY BREAST CANCER

Trastuzumab is a **monoclonal antibody** that binds to the extracellular domain of the HER2 / neu receptor leading to the suppressing of its signaling activity. HER2/neu receptor, which is commanded by the **c-erb B2** gene, plays an important role in the growth and replication of normal cells. Four HER receptors have been identified and they belong to the family of tyrosine kinases. Each of them includes an extracellular domain that commands an intracellular signaling pathway. In one fifth of breast cancer in humans, the HER2 receptor (one of the four HER receptors) is amplified and overexpressed, which means that multiple copies of the gene are present on the chromosome 17 and that multiple receptors are found on the cellular membranes, leading to **the rapid progression and growth of cancer**. Clinically, HER2 positive breast cancers are more aggressive and associated to a worse prognosis.

Trastuzumab suppresses the HER2 expression, causing a cell cycle arrest, reduction of angiogenesis and antibody-dependent cell-mediated cytotoxicity (ADCC). It presents, then, an antitumor activity. HER2 positivity may be detected by two ways: Immunofluorescence classifying the expression from 0 to 3+, and FISH classifying the tumor as positive or negative. The two techniques are complementary in some clinical conditions and are used concomitantly.

Trastuzumab started to be used, in the 90s, in the treatment of metastatic breast cancer, improving significantly the survival of this subgroup of breast cancer patients. Viani, in 2006, collected **5 good randomized clinical trials** comparing Trastuzumab to placebo in an adjuvant setting, and published his results in a meta-analysis. The trials proved that Trastuzumab leads to a reduction in the mortality rate, the recurrence rate, the DFS and the overall survival.

However, Trastuzumab is associated to an increase in cardiac heart failure, especially when associated to anthracyclines, and to an increase in brain metastases of unknown explanation.

The benefit of Trastuzumab has been noted independently from the nodal status and the hormone receptors status of the HER2 positive patients, which encourages its wide use in all these categories.

Trastuzumab is normally administered for a period of 12 months, following adjuvant chemotherapy and radiotherapy. Other protocols are under investigation.