

## Breast Cancer. A Bit of History and Past and Current Situation in Argentina

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## 1. Introduction

According to data from the World Health Organization (WHO), breast cancer represents 16% of all cancers in female patients and for years, it seems to be growing in terms of its frequency.

It is estimated that 1 in 8 women will have breast cancer in their lifetime and this is the main reason why women should have their breasts evaluated regularly.

Treatments for breast cancer have changed considerably in the last 40 years [1].

In the 1960s, radical mastectomy was the only available option and did not differentiate by type of cancer, later the use of tamoxifen (figure 1) was discovered as a therapeutic alternative to chemotherapy in some subtypes of breast cancer in the 1980s.



Figure 1: Nolvadex ® tamoxifen 10mg. ICI PHARMA

The implementation of early detection programs for breast cancer in our country was a milestone, since with this it was possible to detect cases in the initial phases, achieving a direct improvement in the survival rates of the patients.

In Argentina, there are more than 5,800 deaths per year from breast cancer. However, mortality from breast cancer (in our country) has decreased steadily and statistically significantly since 1996. That is, although the number of cases detected is higher, the mortality rate decreases since this type of cancer is possible to be cured if caught early.

In the country there is a great difference in the mortality rate between the different regions. The highest adjusted rate was registered in the states of San Luis, Mendoza, Misiones and in the Federal Capital; while the lowest corresponds to the states of Santiago del Estero, Jujuy, La Rioja, Santa Cruz and Tierra del Fuego.

To get where no one can go and offer a possibility to those women who don't have it, LALCEC (Argentine League Against Cancer) and AVON Cosmetics travel all over the country with the mobile mammography machine. For 20 years, this tour has been carried out during which free mammograms are performed for women of at-risk age and without the possibility of access to the radiological study [2].

## 2. Trastuzumab

In 2004, the first targeted treatments began to appear, more efficacy and fewer side effects for patients.

Trastuzumab is an anticancer drug. It is usually used to treat a type of breast cancer called HER2 neu +++ (positive triple cross) breast cancer. It can also be used to treat certain cancers of the stomach or / or esophagus that have spread.

Trastuzumab only works when cancer cells have high levels of a protein called human epidermal growth factor receptor 2 (HER2). You will first have tests to find out if Trastuzumab is an appropriate

treatment. It can also be used to treat other types of cancer as part of a research trial (figure 2).

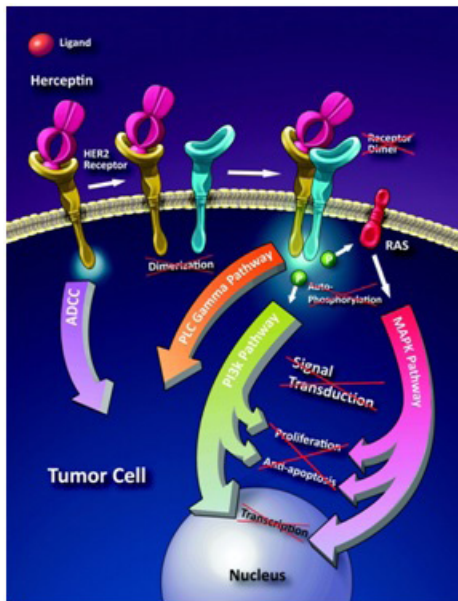


Figure 2

### 3. What is Trastuzumab and How Does it Work?

Trastuzumab is in a group of anticancer drugs called monoclonal antibodies. Monoclonal antibodies are sometimes called targeted therapies, as they work by targeting specific proteins (receptors) on the surface of cells [3].

Some types of cancer have high levels of a protein called human epidermal growth factor receptor 2 (HER2) on the surface of their cells. These are called HER2-positive cancers. The extra HER2 receptors stimulate cancer cells to divide and grow. Trastuzumab binds to the HER2 protein and blocks the receptor. This prevents cells from dividing and growing.

There are different tests to measure HER2 levels in cancer cells. These tests are done on tissue taken during a biopsy or surgery to remove the cancer.

Trastuzumab is a standard treatment for people with HER2-positive breast cancer. It is given after or at the same time as chemotherapy, to reduce the risk that the cancer will come back. Trastuzumab can also be used to treat breast cancer that has recurred or has spread to other parts of the body (secondary breast cancer). In this situation, it is given either by itself or in combination with chemotherapy and / or hormonal therapy [4].

urrent research in breast cancer is directed towards a personalized and precise oncology, where each patient can be applied the best therapeutic option according to her type of cancer.

#### 3.1. A Little History

I cannot help but remember, after more than forty years of practice, my first patients with breast cancer, true heroines and fighters who put all their strength to defeat this disease when after surgery, ac-

ording to the condition of the armpit, "Adjuvant chemotherapy" was indicated.

According to the existing bibliography and the experience of Italian (Gianni Bonadonna) and American (Bernard Fisher) the standard of treatment was the "CMF" scheme.

For the past 43 years, classic CMF (polychemotherapy with cyclophosphamide, methotrexate, and fluorouracil) has been a milestone in the adjuvant treatment of women with breast cancer [5].

However, after an initial burst of success that lasted just over 10 years, classical CMF has been replaced by "third generation" regimens containing anthracyclines and taxanes.

Questions have been raised in recent years about the true efficacy of adjuvant CMF for specific subgroups of patients, and in particular recent retrospective data support the fact that CMF may have a role in the treatment of patients with triple negative breast cancer.

A possible justification to support this role of CMF can be found in the mechanism of action of the drugs used in the regimen, since triple negative tumor cells may be sensitive to alkylating agents that cause breaks in the DNA helical double helix. The lesson learned from the CMF could lead us to identify new drug combinations that could include the optimal chemotherapy backbone for triple negative breast cancer, such as platinum compounds or alkylating agents or poly (ADP-ribose) polymerase inhibitors [6].

The determination of Hormone Receptors (probably the first tumor markers, with diagnostic and prognostic value) was a procedure that very few centers performed in Argentina [7].

During the same surgical procedure, a relative of the patient (husband, son or other) had to be present with a container of Styrofoam with ice dry ... (it was only available in ice cream parlors open "all year round") to place a piece of the specimen there - RH are thermolabile - and take it quickly to the few laboratories that processed the sample and after seven to ten days, the hormonal status of this patient and her tumor were reported. During the early years of the 1970s, only HR was made in the Federal Capital (today CABA)

At the end of this path, we had a pathological anatomical diagnosis, a number of metastasized axillary lymph nodes, and a result of the LR.

The patients were pre or postmenopausal, with positive or negative armpit and RH + or -, according to these parameters we did CMF, CMF + Rt.; CMF + Rt. + Ht.

Already, moving forward in time, during these 25 years, although it is true that there is an increase in the incidence of breast cancer with about 1.7 million cases diagnosed per year, I have already mentioned that both in our country and in the rest in the world, this increase has been due to "screening" programs that allow the detection of this pathology in its earliest stages, where the disease is more easily manageable and with fewer side effects on patients. This early identification of the disease, the improvement in its

classification and the advent of more effective treatments has resulted in a significant reduction in mortality from breast cancer.

The great awareness of the population has promoted the investigation of this pathology, this type of cancer being a precursor when it comes to implementing new results generated in laboratories and that later they have been implemented in the clinical practice of other tumor types such as the improvements techniques of early visualization of the disease, new surgical methods and

the implementation of precision or personalized medicine protocols that make it possible to identify the best treatments for each patient.

Technological advances in images have made it possible to improve breast cancer "screening" through digital mammograms that have high sensitivity and allow the identification of lesions in women under 50 years of age, making screening programs more useful.

On the other hand, and in a very significant way, the improvement in the surgical techniques of mastectomy, surgery "in less" or conservative, determination of the "sentinel node" and in the options of breast reconstruction has allowed to efficiently eliminate the tumor, limiting the impact physical and psychological of the patients.

Radiation therapy plays a key role in the treatment of breast cancer, this technique has made great progress in the last 25 years, reducing toxicity and adapting to the patient's anatomy, which has resulted in an improvement in quality of life of patients.

The completion of the sequencing of the human genome in 2003 and the development of technology to carry out this titanic project had a radical effect in addressing a large number of diseases, including breast cancer. (figure 3)

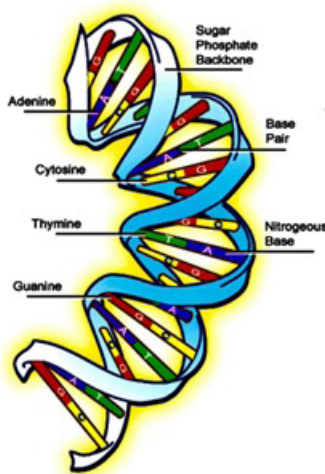


Figure 3

The possibility of identifying the specific alterations of each patient has made it possible to classify and diagnose breast cancer more efficiently, being able to divide this disease into 10 subtypes different with different prognosis and therapeutic implications, but also to identify and develop targeted treatments for recurrent breast cancer disorders.

Precision medicine or personalized treatments have been a revolution in this pathology, allowing a high number of women to benefit from more effective and less toxic treatments. In this regard, the development of "genomic platforms" has been a fundamental advance., there are several, we are going to describe one of them.

### 3.2. Genomic Platforms

The Oncotype DX test is a 21-gene test that predicts the likelihood of benefit from chemotherapy and the distant 10-year risk of recurrence to inform adjuvant treatment decisions in certain women with early-stage invasive breast cancer.

### 3.3. The Oncotype DX Test

Supports treatment decisions — The Oncotype DX test has been incorporated into the ASCO®, NCCN®, St. Gallen and ESMO clinical practice guidelines.

Informs medical decisions and improves confidence in treatment decisions for doctors and patients — Studies suggest that the test results changed treatment decisions for breast cancer in about 30% of cases.

Offers expanded clinical utility — Reports now include quantitative values of ER, PR and HER2

The clinical value of the Oncotype DX test was shown in clinical studies involving about 4,000 patients.

More than 900,000 patients around the world have received the information provided by the Oncotype DX test

More than 19,000 physicians have requested the Oncotype DX test in more than 70 countries

## 4. Clinical Utility

### 4.1. The Oncotype DX test provides information on clinical experience:

For pre- and post-menopausal women with hormone receptor-positive node-negative invasive breast cancer.

For postmenopausal women with node-positive, hormone receptor-positive invasive breast cancer

The challenge for the coming years is focused on the resistance of tumors to the treatments and protocols used, due to their high cost and the limited access of many countries to the latest advances in breast cancer research. (figure 4).

## Oncotype DX Breast Recurrence Score<sup>®</sup> Report Node Negative

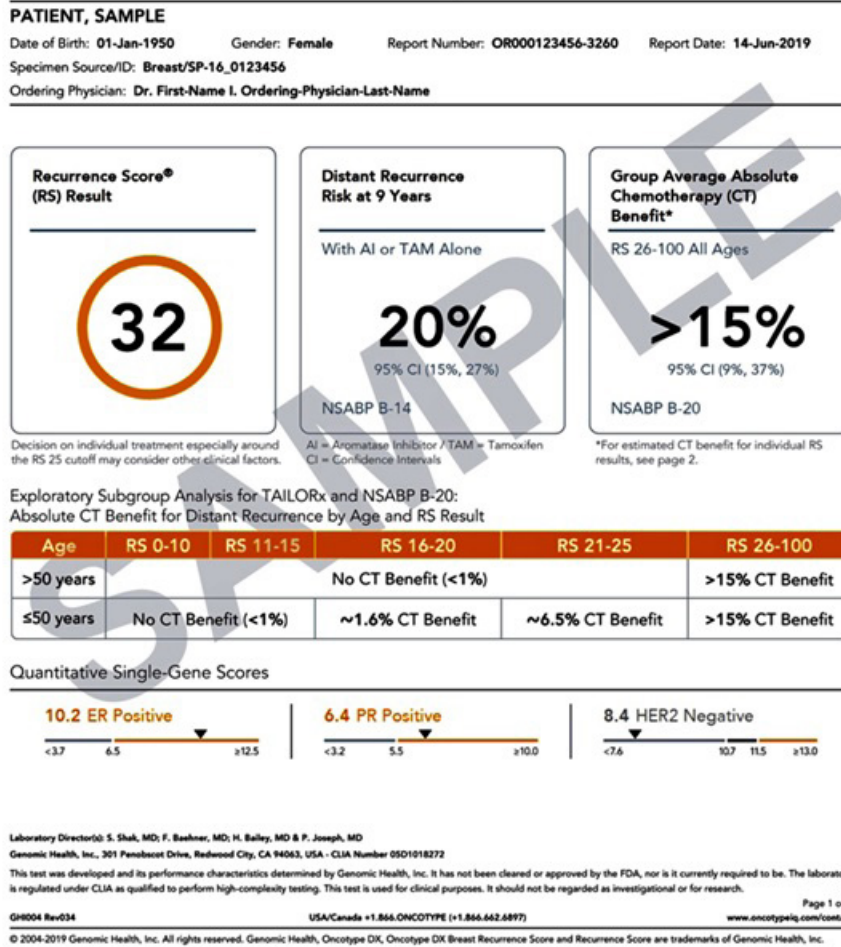


Figure 4

### 5. Conclusion

In conclusion, I have wanted to provide an absolutely personal vision of more than forty years of treating patients with breast cancer and personally I am pleasantly surprised by the advances in the diagnosis and treatment of this frequent disease, definitely mortality in advanced and potentially curable patients today, even with metastases as surely every oncologist with years of experience has lived.nb.

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