CAN WE TREAT LOCALLY OPERABLE BREAST CANCER WITHOUT SURGERY? IS PRIMARY DEFINITIVE HORMONE THERAPY A VALID ALTERNATIVE FOR OPERABLE HORMONE SENSITIVE BREAST CANCER?

Vasco Fonseca & Zacharoula Sidiropoulou
Medical Oncology and Surgical Department of Centro Hospitalar de Lisboa Ocidental Lisbon, Portugal
Background

- Existing guidelines inform treatment decisions based on tumor biology and staging:
  - Surgery is most often recommended
  - Hormone therapy (HT) in the neoadjuvant setting is accepted but seldom used
- In our clinical practice, we observed that not every patient benefits the same way from complex treatments

*We treat people not tumors!* *(quality of life, disease control & mortality rates do matter)*
Defining the problem

2-4% of our breast cancer patients (mostly elder women) either refuse surgery or have a poor general health status.

Not all patients benefit from complex treatments in terms of Quality of Life (QoF), disease control, and Mortality rates.

Hormone Therapy (HT) is rarely proposed as an alternative to surgery.

Tumor microenvironment has been mostly disregarded.

*We advocate that the ideal treatment should be customized to each specific patient with a specific tumor*
Questions to be answered  EF Breast Cancer Patients Trial in a Better Way Faculty Human Kinetics
University of Lisbon / West Lisbon Hospital Centre (V. Fonseca; P. Sarmento; L. Sardinha)

- How can we Evaluate, Follow, and Support Breast Cancer Patients, in a Better Way?

- What kind of physical and cognitive evaluation should we offer to Breast Cancer Patients?

- How can we use data on patient’s Kinetics, physical condition, and cognitive status, in the clinical practice?

- How can we assess the practical impact of such data, in the clinical practice?
Proposed solution

1. Consider changes in clinical practice:

- Assess the introduction of new variables in patient’s evaluation: Performance Status, The G8 screening questionnaire, Charlson Comorbidity Index (CCI)

- Develop an algorithm to facilitate the incorporation of such new variables

- Ask patients to contribute to the validation of the algorithm
Proposed solution

2. Consider changes in clinical practice:

Validate our strategy of beginning systemic neoadjuvant hormonotherapy (NA-HT) immediately after histologic diagnosis (Valid for most patients. Exception: patients with an indication for neoadjuvant chemotherapy)

Ensure educated options from patients
Why this option?

1. **Avoids undertreatment**: diagnosed BC patients should not stay without any treatment, during the period of staging assessment and while waiting for surgery.

2. **Avoids overtreatment**: since tumor biology changes after HT, with expected impact on overall treatment aiming at protecting those patients who respond from overtreatment.

3. **Creates a window of opportunity** to assess if surgery is the best option for each specific case, while patients are receiving some treatment (some times the best option is a systemic approach).
In Luminal Breast cancer, we need to:

1. Contribute with supplementary information to guidelines: Current guidelines allow the use of NA-HT but the ideal duration is not clearly defined.

2. Consider transforming NA into primary and unique therapy, for a defined subgroup of patients
Our experience – ongoing clinical trial

HoTBreast trial NCT03111615 - phase III interventional study  V. Fonseca/ Z. Sidiropoulou

• Consists on the use of pre-operative hormone treatment (HT) in Luminal-like operable BC patients.
  - Aim at observing the changes in the biology of the tumor and its microenvironment after the introduction of HT.
  - One of the arms compares the use NA-HT with HT
Some results

Aspirin and breast cancer?
Or Too Cheap to be Good?

Vasco I onseca MU and Zacharoua Sidiropoulou MU

What Science Teaches: Aspirin plays the role of an anti-inflammatory controller but it is not clear what the relation between chronic inflammation processes and BC is.

The results of the latest meta-analysis supported the presence of inverse associations between aspirin use and the risk of overall breast. Several biological mechanisms through which aspirin could reduce the risk of cancer are investigated:

➢ Aspirin and other NSAIDs inhibit the activity of the enzyme COX-2, responsible for the synthesis of prostaglandins. COX-2 has been reported to be overexpressed in many cancers and participates in key cellular activities, like cell proliferation, apoptosis, angiogenesis, and metastasis.

➢ Aspirin could activate signalling pathways, which trigger apoptosis in neoplasia.

➢ Aspirin might induce gene selection and modulate mitochondrial voltage dependent anion channels (VDACs) to reduce the risk of cancer progression and metastasis.

➢ Aspirin inhibits cell growth in all cancer cell lines regardless of mutational background.

What Clinical Practice Teaches: In clinical practice there exist clear guidelines for the use of aspirin in colorectal cancer but no such guidelines for the use of aspirin in breast cancer patients. We have used aspirin in breast cancer patients in the metastatic setting and neoadjuvant setting after informing them about the benefit of this strategy, and have observed some very good responses in both settings. We can report some cases of a locally advanced (cT4N1Mo) luminal type breast cancer patients that refused surgery and have obtained complete response through the association of aspirin and hormonotherapy. We can also report cases of metastatic breast cancer patients, who, five years after initial diagnosis of lung and hepatic disease, have obtained disease stabilization through the use of chemotherapy and hormonotherapy complemented by aspirin.
HOTBreast-Asp / Trial  V. Fonseca ; Z. Sidiropoulou

- Regular and low-dose aspirin, other non-steroidal anti-inflammatory medications and prospective risk of HER2-defined breast cancer: the California Teachers Study

- Repurposing drugs in Oncology / low dose aspirin / Aspirin chemotherapeutic and chemopreventive agent

- One of the arms compares the use NA-HT with NA-HT + aspirin

- Disease progression and QoL will be assessed from clinical and imaging (ultrasound) follow-up
Secondary objectives

To understand if local disease responds the same way as the systemic one

Better define parameters for HT in the neoadjuvant (NA) setting, in luminal breast cancer

Setup a strategy to communicate information about the option HT-NA in luminal breast cancer, for an educated decision from patients
From our experience

In situ breast cancer

- Watch and wait
- USC/Van Nuys Prognostic Index - useful tool in decision making process for patients diagnosed with DCIS
- Some patients may benefit from hormonetherapy
- Radiologic interventions can be an option

Her2 + Breast Cancer

- Age: not a factor when assessing the use of Trastuzumab
- DanaFarber Regimen: extendable in most cases, and anthracyclines can be avoided

Metastatic Disease

- QoL is the most important factor
- Assess oral therapies and low dosages for better QoL
From our experience

Factors that may strongly impact quality of life, survival and longevity:

• Prescribing physical exercise adapted to patient’s condition
• Prescribing cognitive exercises
• Treatments for bone health
• Encouraging social and personal relationships
In short

- Changes in clinical practice should be considered, by introducing more variables aim at customizing treatment.
- NA-HT may be important as an early / definitive treatment.
- Patients should be clearly informed and these informed options should be respected.
- HT + aspirin might be an option.
- Prescribing physical and cognitive exercises, and encouraging relationships will improve patient’s survival rates and QoL.
Take home message

IN BREAST CANCER
Eldrely breast cancer patient has the same rights as the young one (screening, diagnostics, trials and new drugs) just depending on her clinical status. It is not an exclusively dependent age decision.

Early diagnosis remains critical

The treatment option should be discussed with the patient (clearly informed) in order to avoid overtreatment.

Sometimes surgery can be avoided
Thank you for your attention
Disclosure

I do not have any conflict of interest to declare.