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Short Communication

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Pre-operative Early Hormonotherapy the New Gold Standard for Operable Luminal Breast Cancer

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Even though it is not yet a universally accepted, in our view, the best clinical practice in the case of operable luminal breast cancer is to begin systemic neoadjuvant hormonotherapy (HT) immediately after histologic diagnosis for the majority of patients. This strategy does not apply to patients with an indication for neoadjuvant chemotherapy.

There are three main convincing reasons for changing this practice in the real world of breast cancer clinical management.

The first reason is that it avoids undertreatment, which means that it does not leave a diagnosed BC patient without treatment, even if just for the period staging is taking place.

The second reason is that it avoids overtreatment. Since tumour biology changes after HT, leaving a window of opportunity, this fact should have an impact on the definitive treatment, protecting those patients who respond from overtreatment.

The third reason is that it allows us to implement an early treatment. This is to say that patients that don't want to go or cannot go to surgery can be treated in an adequate way, sometimes the ideal one, with just the systemic approach.

Taking into account that in our clinical practice the average waiting time between diagnostic biopsy and surgery is 1 month – and in some cases is up to 3 months or more – and that in developing and underdeveloped countries, the time frame in between diagnosis and start of treatment is extensive, this short period of HT might be able to reduce tumour proliferation index and can be included in clinical guidelines [1]. Furthermore, in cases of molecular surrogate "downstage", definitive treatment should probably be based on the operative anatomy pathological result and not on the biopsy result. Indeed, we expect to reduce overtreatment in a large percentage of patients if the results of changes in a tumor's biology are taken into account.

The Alternate and PowerPink trials, among others, propose that changes in ki67 should be taken into account in treatment decisions [2,3]. The Poetic trial also confirms that changes in ki67 are obtained after the introduction of early HT [4]. In the trial we have designed, HoTBreast, we expect to confirm changes in tumor biology after the early introduction of hormonotherapy with anastrazole [5]. The main ethical question addressed by the HoTBreast trial is that should we offer this window of opportunity hormone treatment to all patients, even though we know that this strategy is not supported by the current guidelines for BC [6]. We accept that the window of opportunity time for early HT can be adjusted to the way that different Breast Units work, adapting to their average times between diagnosis and start of treatment. In this way, the strategy is not designed solely for Breast Units of excellence with a short period from diagnosis to surgical treatment.

A few obvious questions arise from the third question: can we treat operable BC without surgery? Is primary definitive HT a valid alternative for operable hormone sensitive BC?

In our clinical practice, we propose primary HT in luminal like breast cancer cases, to specific patients, such as those with a bad performance status or those that refuse surgery. The majority of these patients are elderly and are sometimes afraid of the treatment and of changes in their body image.

There are guidelines which inform treatment decisions based on tumor biology and staging, but we need more precise algorithms that also incorporate and give a specific weighting to the different factors affecting a patient´s general condition. Not all patients benefit from very complex treatments in terms of quality of life, disease control and mortality rates. We advocate that the ideal treatment should aim not just to treat the tumor but to be the ideal treatment for the specific tumor in the specific patient. Current guidelines permit the use of HT in the NA setting. The ideal duration, however, is not clearly defined. In a subgroup of patients this NA could be transformed into primary and unique therapy [7].

We defend a global paradigm shift in BC treatment that allows the simplest form of treatment to become the best approach, and promotes the uniformization of breast cancer treatment around the globe, ensuring that specific centers / or whole countries that have longer times until treatment initiation don't prejudice patients due to the shortcomings of the health system in question.

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