



ADJUVANT THERAPY FOR BREAST CANCER STAGE I (HER-2 POSITIVE) : EXPERIENCE IN THE "HOSPITAL ONCOLOGICO GENERAL SOLON ESPINOSA AYALA" SOLCA QUITO-ECUADOR

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ABSTRACT

Objectives: to describe the demographic variables of breast cancer stage I HER-2 positive and to assess the response to adjuvant therapy with different protocols.

Methods: A descriptive analysis of women over 18 years old treated with adjuvant chemotherapy with or without trastuzumab, assessing overall survival and the survival estimation was performed by Kaplan Meier method and compared with Log Rank test.

Results: Adjuvant therapy was performed in 22 patients stage I, IA (19 / 86.4%) and IB (3 / 13.6%), a global survival was reached until December 2018 of 65.5 months, however, according to the treatment, trastuzumab as monotherapy had a survival of 70 months, TCH=40 months, AC=76 months, AC-H=61.5 months, AC-TH=75 months with $p = 0.004$ in terms of immunophenotype HER-2 (positive) vs HER-2 (negative)/HR (hormonal receptor)= were 68.4 months vs 63.3 months $p = 0.59$

Conclusion: Although the main weakness of this study is that it is a retrospective trial, it is striking that several treatment options have been provided to stage I, however it must be analyzed that 10 patients were treated only with trastuzumab, reaching a survival of 70 months, while the remaining 12 patients were divided into several treatment options, although the AC scheme reports 76 months of survival corresponds to a single patient, for this reason is necessary a institutional or national guideline for treatment cancer in Ecuador.

KEYWORDS : breast, cancer, adjuvant, HER2, trastuzumab, Quito, Ecuador

INTRODUCTION

The breast cancer in Ecuador has had an important increase in the last three decades; according to the national registry of tumors it occupies the first place of incidence and the third one in mortality (1) (2)

Women with breast cancer HER-2 positive have a higher risk of progression and death, which is why strategies have been developed to block this signaling pathway allowing control of this biologically more aggressive variety, in Ecuador it has been possible to determine in previous studies an overexpression or amplification of HER-2 in a range of 11.58% -14.3%, with a greater presence in women over 60 years of age and of a Latin American racial group with little overexpression in indigenous or Afro-descendant women. (3,4)

Adjuvant therapy with trastuzumab has shown significant increase in overall survival and disease-free survival in relation to chemotherapy alone.

The objectives of this research are to describe the demographic variables, and to assess the response to trastuzumab in adjuvant clinical stage I; as well as disease-free survival.

METHODOLOGY

Oncology clinical records of the "Hospital Gral. Solón Espinosa

Ayala" of 1010 women was reviewed during the years 2010 and 2015 with the diagnosis of breast cancer and as the last reference date December 2018, of women with breast cancer stage I treated with adjuvant therapy, having a total sample of 22 patients.

The cases were identified through the National Registry of Tumors of women older than 18 years old and confirmed diagnosis of breast cancer stage I with overexpression or amplification of HER 2.

A general descriptive analysis of the group of selected patients was performed, overall survival, survival estimation was performed using the Kaplan Meier method and survival functions were compared using the Log Rank test.

The information obtained from the digital medical records was analyzed using the SPSS statistical package.

RESULTS

Adjuvant therapy was performed in 22 patients with stage I, IA (19 / 86.4%) and IB (3 / 13.6%), of which 11 patients younger than 50 years old and 11 patients older than 50 years old; 10 patients were treated with trastuzumab alone, 12 patients were treated with a different treatment scheme that included chemotherapy alone or chemotherapy and then trastuzumab, as well as sequential and recurrent treatment; data described in Table 1.

Table 1.

| Variable | | N | % |
|---------------------|----------------|----|------|
| Age | < 50 | 11 | 50 |
| | > 50 | 11 | 50 |
| | | 22 | 100 |
| Stage | IA | 19 | 86.4 |
| | IB | 3 | 16.6 |
| | | 22 | 100 |
| PATHOLOGY | DUCTAL | 20 | 90.9 |
| | LOBULAR | 1 | 4.5 |
| | PAPILAR | 1 | 4.5 |
| | Total | 22 | 100 |
| HISTOLOGICAL DEGREE | 1 | 4 | 18.2 |
| | 2 | 15 | 68.2 |
| | 3 | 3 | 13.6 |
| RACE | LATINOAMERICAN | 17 | 77.3 |
| | INDIGENOUS | 3 | 13.6 |
| | AFRO ECUADOR | 2 | 9.1 |
| | Total | 22 | 100 |
| TREATMENT | Trastuzumab | 10 | 45.5 |
| | *TCH | 2 | 9.1 |
| | **AC | 1 | 4.5 |
| | AC-H | 7 | 3.8 |
| | AC-TH | 2 | 9.1 |
| | | 22 | 100 |
| immunophenotip | HER2+ | 10 | 45.5 |
| | RE***/HER2+ | 12 | 54.4 |
| | | 22 | 100 |

* TCH (Docetaxel/Carboplatin/Trastuzumab); ** (Doxorubicin/ Ciclofosfamid) H(Trastuzumab)
 ***HR hormonal receptor

Regarding survival, it was observed that patients who received adjuvant therapy only with trastuzumab had a survival of 70.7 months HR 3.36 IC 95% (60.1-77.2 months); and although we have a significant $p=0.004$, we must appreciate that there are patients that exceed this time of survival with AC or AC-TH scheme, however the sample is very poor of 1 and 2 patients respectively. Data reported in Table 2.

Table 2.

| THERAPY | months | Std. Error | IC 95% |
|-------------|--------|------------|--------------|
| Trastuzumab | 70,7 | 3,4 | (64,1 -77,3) |
| TCH | 40,0 | 2,0 | (36,1-43,9) |
| AC | 76,0 | 0,0 | (76 -76) |
| AC -H | 61,6 | 8,0 | (45,8 -77,3) |
| AC-TH | 75,0 | 3,0 | (69,1-80,9) |
| Overall | 65,6 | 3,5 | (58,7- 72,5) |

Log Rank 15.11; $p=0.004$

With regard to clinical stage, there is a marked difference between IA and IB, of 64.4 months vs 73 months respectively, however only 3 patients are seen in stage IB, for which we report a $p=0.943$

Finally, in terms of HER-2 positive vs HER-2 luminal, HER-2 positive represents a survival of 68.4 months vs 63.3 months, $p=0.59$

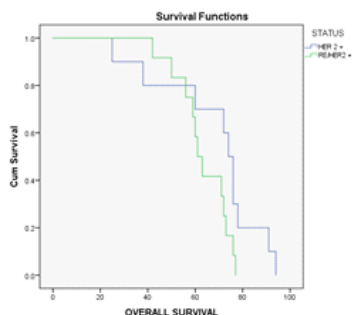


Figure 1.
 Log Rank: $3.56 p=0.59$

DISCUSSION

Since FDA approved trastuzumab in the adjuvant setting in 2006, several trials have studied the benefit of adding trastuzumab to chemotherapy in the neoadjuvant and adjuvant setting.

The first studies with Trastuzumab NSABP B-31 and NCTG N9831 showed an increase in the disease-free period from 75.2% to 84%, whereas in the Breast Cancer International Research Group 006 trial (BCIRG-006) (5-10), Trastuzumab was evaluated in conjunction with docetaxel and carboplatin, drugs with which he had previously shown to have synergy, demonstrating in the same way increased effectiveness and with the HERA test at one year showed equal figures, in our institution we can appreciate a time of survival 5.8 years for stage I, in treatment only with trastuzumab, even though is not an equal group this data is important to be taken into account for future research, however we should not ignore the fact of the important benefit of adding a taxan to trastuzumab demonstrated already in several of the studies previously mentioned with greater sample.

Regarding demographic analysis, the group of indigenous or Afro-descendant patients has a lower expression, data similar to those reported in previous studies in our institution. (3,11)

In conclusion Trastuzumab is our institution shows clinical and statistical advantages so it should continue to be used in this group of patients, however guidelines should be created for clinical practice at the country level and in this way offer a standard of treatment and not over treating patients or undertreating.

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