TREATMENT PATTERNS AND PROGNOSTIC FACTORS OF LOCALLY ADVANCED OR METASTATIC HR+ / HER2- BREAST CANCER IN ARGENTINA

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ABSTRACT

OBJECTIVES: The objective of this study is to describe treatment patterns and prognostic factors of patients with advanced or metastatic HR+/HER2- breast cancer in Argentina.

METHODS: Patients with HR+/HER2- locally advanced or metastatic breast cancer who received endocrine therapy (ET), chemotherapy (CHT) or radiotherapy from 2013 to 2018 were selected from the Instituto de Especialidades Médicas clinical database, which includes individuals covered by the social security. Information collected included clinical stage, treatment, response to treatment and survival. Analysis was conducted stratified by initiation of treatment before or after January 2016.

RESULTS: 230 patients were included; 32 had started treatment after January 2016. Mean age was 56.4 (SD 11.9) years. In the group that started any treatment after 2016, 31% received CDK4/6 inhibitors, 76% ET and 52% CHT as first-line therapy (66% received more than one treatment). The most prescribed combination was palbociclib with letrozole (21%). The most prescribed first-line CHT was paclitaxel (40%) and doxorubicin (40%). In second-line therapy, CHT increased to 60%. In those patients who started treatment before 2016, first line therapies were CDK4/6 inhibitors 4%, ET 62% and CHT 61% (39% of those who received two or more treatments). The most frequent first-line CHT was paclitaxel (33%) and the most frequent ET was anastrozole (46%). Sensitivity to hormonotherapy (defined as more than 36 months from the end of ET to beginning of first-line, 20% of all cases) and resistance to previous hormonotherapy (less than 24 months from beginning of ET to beginning of first-line or less than 6 months from beginning of hormone therapy first-line and second-line, 23.0% of cases) were identified as relevant prognostic factors for survival.

CONCLUSIONS: Treatment patterns for advanced or metastatic breast cancer in Argentina are highly heterogeneous and have experienced substantial changes during the last years. The high CHT use indicates an unmet need for care.

BACKGROUND

- Breast cancer (BC) is the most frequently diagnosed cancer in women.
- Argentina is one of the Latina American countries with the highest age-standardized incidence rates of BC (73.0 per 100,000, IARC 2020).
- Clinical guidelines for the treatment of metastatic breast cancer show relevant treatment variability (Cardoso et al, 2018; Carvajal et al, 2018).
- Given the appearance of new treatments, locally advanced or metastatic breast cancer treatment has experienced substantial changes in the last years.

OBJECTIVE

The objective of this study is to describe the treatment patterns and prognostic factors of patients with advanced or metastatic HR+ / HER2- breast cancer in Argentina.

METHODS

Patient selection

- The criteria for inclusion in the sample were:
  - Diagnosis of Advanced or Metastatic Breast Cancer
  - Positive Hormone Receptors (at least one, Estrogens or Progestogens)
  - Oncogen Her-2 negative.
  - In treatment for relapse or advanced breast cancer during the period 2013 to July 2018
- Patients were selected from the Instituto de Especialidades Médicas S.A. (IEMSA) clinical database, which includes information about individuals under several insurance providers ("Obras Sociales" and "Empresas de Medicina Prepaga").
- Information collected included clinical stage, treatment, response to treatment and survival.

Patient Groups

To analyse recent changes in treatment patterns, analysis was stratified date of initiation of treatment in the advanced setting (before or after January 2016, the date was chosen given the availability of CDK4/6 inhibitors).

- **Group 1 (n=32, 14%):** patients who started any first-line treatment (chemotherapy, hormonal therapy or radiotherapy) after January 1, 2016 .
- **Group 2 (n=198, 86%):** patients who started any first-line treatment (chemotherapy, hormonal therapy or radiotherapy) before January 1, 2016.

Statistical analysis

Patient characteristics and clinical information were described. Comparisons were conducted using the Chi-square test for categorical variables and Wilcoxon-Mann-Whitney or Kruskal-Wallis tests for numerical variables.

Prognostic factors

Survival analyses using the Kaplan Meier estimation were used to study the influence of prognostic factors on survival. Patient survival was calculated from the time from the initiation of first line therapy to death.

The prognostic factors analysed were:

- Sensitivity to hormonal therapy: Time from beginning of adjuvant hormonal therapy to beginning of first-line therapy more than 36 months.
- Resistance to hormonal therapy: Time from beginning of adjuvant hormonal therapy to beginning of first-line therapy < 24 months or time from beginning of hormonal therapy first line and the beginning of second-line therapy < 6 months (Cardoso 2014).

All analyses were performed using SAS (version 9.4).

RESULTS

Table 1: CLINICAL AND SOCIODEMOGRAPHIC CHARACTERISTICS

Clinical and sociodemographic baseline characteristic	Overall sample (n = 230)	Group 1* (n= 32)	Group 2* (n= 198)
Age (mean, (std)) [min – max]	56,4 (11,9) [30 - 89]	52,9 (12,4) [35 - 82]	57 (11,8) [30 - 89]
Body Surface (mean, std) [min – max]	1,69 (0,08) [1.51 - 1.91]	1,70 (0,08) [1.51 - 1.88]	1,69 (0,08) [1.51 - 1.91]
Initial stage			
I/I(bilateral)	21 (90,3)%)	-	21 (10,7%)
II/II-III/local	104 (45,8%)	7 (22,6%)	97 (49,5%)
III/III (bilateral)/Locoregionalmente advanced, bilateral, locally advanced, locally advanced bilateral	64 (28,2%)	14 (45,21%)	50 (25,5%)
IV / IV(inflammatory)	38 (16,7%)	10 (32,32%)	28 (14,3%)
Situation of patient at inclusion			
Died	79 (34,5%)	6 (18,8%)	73 (37,1%)
Free of Desease / Control	2 (0,9%)	-	2 (1%)
Lost-to-followup	73 (31,9)%	6 (18,8%)	67 (34%)
Under Treatment	75 (32,8)%	20 (62,5%)	55 (27,9%)

***** Group 1: patients who started treatment after January 1, 2016;
Group 2: patients who started treatment before January 1, 2016

Clinical and sociodemographic characteristic	Overall sample (n=230)	Group 1 (n= 32)	Group 2 (n= 198)
Current Stage			
III / locorregional	10 (4,6%)	3 (11,1%)	7 (3.7 %)
IV	195 (89,54%)	23 (85,2%)	172 (90,1%)
Other	13 (6,0%)	1 (3,7%)	12 (6,3%)
ECOG			
0	178 (78,4%)	17 (54,8%)	161 (82,1%)
1	41 (18,1%)	12 (38,7%)	29 (14,8%)
2	6 (2,6%)	1 (3,2%)	5 (2,6%)
3	2 (0,9%)	1 (3,2%)	1 (0,5%)
Sensitivity to hormonal therapy			
No	107 (80,54%)	9 (100%)	98 (79%)
Yes	26 (19,6%)	0 (0%)	26 (21%)
Resistance to hormonal therapy			
No	124 (77%)	3 (23,1%)	121 (81,8%)
Yes	37 (23%)	10 (76,9%)	27 (18,2%)

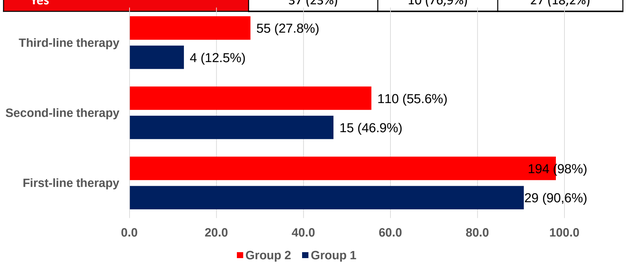


Table 2: TREATMENTS IN FIRST LINE-THERAPY

Parameter	Value	Group 1 (n=29)	Group 2 (n=198)
First line-therapy: Chemotherapy*	Yes	15 (51,7%)	119 (61,3%)
First line-therapy: Hormonal therapy*	Yes	22 (75,9%)	120 (61,9%)
First line-therapy: Radiotherapy*	Yes	4 (13,8%)	28 (14,4%)
First line-therapy: CDK4/6 Inhibitors*	Yes	9 (31%)	8 (4,1%)
Total number of treatments in 1st line therapy	1	10 (34,5%)	119 (61,3%)
	2	17 (58,6%)	69 (35,6%)
	3	2 (6,9%)	6 (3,1%)
Combination of treatments in first line-therapy	Only Chemotherapy	7 (24,1%)	65 (33,5%)
	Only Hormonal therapy	3 (10,3%)	51 (26,3%)
	Only Raditoherapy	-	3 (1,6%)
	Chemo & Hormonal	6 (20,7%)	42 (21,7%)
	Chemo & Radio	-	6 (3,1%)
	Hormonal & Radio	2 (6,9%)	13 (6,7%)
	Hormonal & CDK4/6	9 (31%)	8 (4,1%)
* Grups are not mutually exclusive	Chemo & Hormonal & Radio	2 (6,9%2)	**6 (3,1%)**

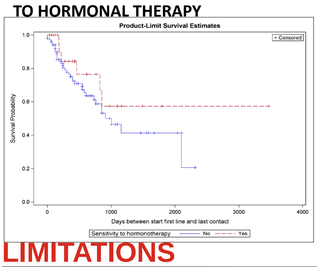
Table 3: TREATMENTS IN FIRST LINE-THERAPY

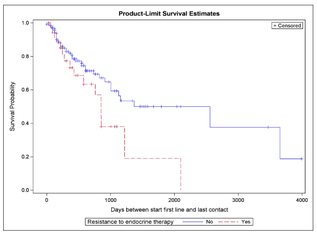
Most frequent treatments in first-line therapy (hormonal therapy, chemotherapy and CDK4/6)	Group 1 (n=29)	Group 2 (n=198)
Palbociclib + Letrozol	6 (20,7%)	5 (2,6%)
Letrozol	-	12 (6,3%)
Anastrazole	2 (6,9%)	36 (18,8%)
AC	2 (6,9%)	10 (5,2%)
Capecitabine	1 (3,5%)	18 (9,4%)
Paclitaxel		10 (5,2%)
Capecitabine + Letrozol		6 (3,1%)
Tamoxifeno		5 (2,6%)
Other	18 (62,1%)	89 (46,86)
TOTAL	**29 (100%)**	**191 (100%)**

Table 4: TREATMENTS IN SECOND LINE-THERAPY

Parameter	Group 1 (n=29)	Group 2 (n=198)
Chemotherapy	9 (60%)	71 (64,6%)
Hormonal therapy	7 (46,7%)	70 (63,6%)
CDK4/6 Inhibitors	3 (20%)	9 (8,2%)
Radiotherapy	2 (13,3%)	8 (7,3%)

Figure 2: SURVIVAL ANALYSIS BY SENSITIVITY AND RESISTENCE TO HORMONAL THERAPY





LIMITATIONS

- This is a retrospective study based on clinical chart data. Due to that some information could not be completed for all patients.
- Sample size is relatively small which makes difficult detailed analysis of some of the variables

CONCLUSIONS

- **Treatment patterns for advanced or metastatic breast cancer in Argentina are highly heterogeneous and have experienced substantial changes during the last years.**
- **Sensitivity and resistance to hormonal therapy are relevant prognostic factors in metastatic cancer.**
- **The high CT use indicate an unmet need for care.**

References:

Cardoso F, et al. ESMO 2nd international consensus guidelines for advanced breast cancer (ABC2). Breast 2014; 23: 489–502.
Cardoso et al. Treatment guidelines for advanced breast cancer. Ann Oncol (2018); 29: 1634–1657
2018. IARC. https://gco.iarc.fr/today/data/factsheets/populations/32-argentina-fact-sheets.pdf. Accessed May 3, 2020
Carvajal et al. Guía de práctica clínica para el manejo del cáncer de mama en estadios tempranos, localmente avanzados y metastásicos November 2018, DOI: 10.24875/j.gamo.M18000161

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