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Real-world data describing the role of chemotherapy in the treatment of HR+/HER2- mBC patients: divergence from evidence-based medicine

Bruce Feinberg, DO[1], Jonathan Kish, PhD, MPH[1], Igoni Dokubo, MD[2], Jeff Wojtynek, PharmD[2], Kevin Lord, PhD, MHS[1]

[1]Cardinal Health Specialty Solutions Dublin, OH; [2]Athenex, Inc., Buffalo, NY

BACKGROUND

- There are 1.7 million new breast cancer cases diagnosed annually worldwide, causing an estimated 500,000 deaths every year.[1]
- Although overall 5-year survival has increased, metastatic breast cancer (mBC) remains incurable with an estimated 5-year survival rate of only 25%.[2]
- The most common breast cancer molecular subtype is hormone receptor positive/human epidermal growth factor receptor 2 negative (HR+/HER2-).
- Over the last two decades, there have been major advances in systemic therapy for mBC, including new targeted therapies for hormone receptor-positive tumors.
  - For HR+/HER2- patients, hormonal therapy is the recommended initial treatment for mBC; cytotoxic chemotherapy is typically reserved for patients in visceral crisis.[3]
  - In 2015, the superiority of cyclin-dependent kinase (CDK) 4/6 inhibitors in combination with aromatase inhibitors (and fulvestrant) for HR+ patients was recognized with the first approval of palbociclib plus letrozole.[4]
- No real-world studies have evaluated treatment patterns in first-line (1L) palliative care for HR+/HER2- mBC patients following the U.S. Food and Drug Administration (FDA) approval of palbociclib.

OBJECTIVES

- To describe the rate of utilization of palliative 1L chemotherapy in the treatment of HR+/HER2- mBC in the United States in recent years.
- To describe the efficacy of single-agent chemotherapy (saChemo), combination chemotherapy (cChemo) and hormonal/targeted (H/T) therapy in 1L palliative care of mBC patients using time to progression to second-line (2L) treatment.

METHODS

Study Design

- Retrospective cohort study of HR+/HER2- mBC patients initiating any 1L palliative treatment identified in the Symphony Health administrative claims database between 01/01/2015 and 10/31/2018.
- Patients were identified as HR+/HER2- using the following criteria:
  - Had to have received an aromatase inhibitor, selective estrogen receptor modulator, estrogen antagonist, luteinizing hormone-releasing hormone analog, CDK 4/6 inhibitor, and/or mammalian target of rapamycin.
  - Did not receive any HER2 targeted therapy.
- Palliative therapy cohorts were categorized as saChemo, cChemo, and H/T.
- The frequency of use of each regimen was reported by age, number of comorbidities, and the presence of visceral metastasis.

Patients

Inclusion Criteria

- Patient had continuous medical and/or pharmacy claims, at least one nondiagnostic inpatient, or two outpatient, six months pre- and six months post-breast cancer diagnosis (174.x, D05.x, D24.x, D48.6x, C50.x).
- At least one claim for lymph node/distant metastatic disease after initial breast cancer diagnosis (196.1, 196.2, 196.5, 196.8, 197.1-197.8, 198.1, 198.6, 198.82, C77.x, c78.x, C79.x).
- Patient had a pharmacy or medical claim (NDC/HCPCS) for any of the following within 45 days after the first claim for metastatic disease:
  - Aromatase inhibitor
  - Selective estrogen receptor modulator
  - Estrogen antagonist
  - Luteinizing hormone-releasing hormone analog
  - CDK 4/6 inhibitor
  - Mammalian target of rapamycin
- Patient ≥18 years old at time of initiation of palliative care.

Exclusion Criteria

- Patient had a medical or pharmacy claim for a selectively targeted HER2 receptor pathway antagonist.
- Patient had a prior claim for another primary care diagnosis or metastatic disease.

Main Outcomes/Measures

- Demographics and clinical characteristics of patients treated with saChemo, cChemo, and H/T.
- Characteristics of HR+/HER2- mBC patient treatment patterns (frequency of use of saChemo, cChemo, and H/T).
- Patient characteristics and treatment patterns were summarized using descriptive statistics (e.g., counts and proportions, measures of centrality and spread) and univariate analyses (e.g., chi-square test).
  - Comorbidities measured were variables constituting the Charlson comorbidity index.
  - Visceral metastasis is defined as metastases of the lungs, digestive, excretory, reproductive, and circulatory systems (see specific ICD-9/10 codes under inclusion criteria).
- Kaplan-Meier method was used to assess the proportion of patients that did not progress to 2L therapy at 6 months.
  - Time to 2L therapy was defined as the time from the first claim for a regimen in 1L palliative therapy until the first claim for the next line of therapy minus one day.
  - Patients were censored on their last date of treatment when no next line of therapy was observed or when there was a gap in claims data >90 days prior to the end of the study date.

RESULTS

Study Cohort Demographics

- There were 2,199,078 patients identified with a breast cancer diagnosis between 01/01/2015 and 10/31/2018 in the Symphony Health administrative claims database **(Table 1)**.
- Using medical and pharmacy claims, 4,317 female patients were characterized as HR+/HER2- mBC patients **(Table 1)**.
- The mean age of the patient cohort was 59.9 years with the greatest percentage of the patients located in the Western part of the United States **(Table 2)**.

Table 1. Attrition Diagram for the Selection of mBC Patients Treated with Chemotherapy

Patients with a breast cancer diagnosis between 01/01/2015 and 10/31/2018
2,199,078
Female patients with a minimum of 6 months of continuous pharmacy and medical claims activity pre- and post-breast cancer diagnosis
1,100,500
At least one claim for metastatic disease: ICD-9/10 codes diagnosis (196.1, 196.2, 196.5, 196.8, 197.1-197.8, 198.1, 198.6, 198.82, C77.x, c78.x, C79.x)
54,167
Initiated any hormonal or chemotherapy within 45 days of first claim for metastatic disease
22,393
Patients with no prior claims for another primary cancer diagnosis or metastatic disease
9,475
Patients not receiving any HER2 target therapy (trastuzumab, ado-trastuzumab etamine, pertuzumab, lapatinib, neratinib)
7,497
Patients characterized with HR+/HER2- molecular subtype metastatic breast cancer
4,317

Demographics & Clinical Characteristics

Table 2. Patient Demographics of HR+/HER2- mBC Patients

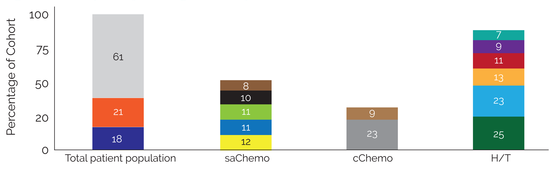
Total patients (n, %)	4,317	
Age at initiation of therapy, years (mean, SD)	59.9	12.0
Payer type (n, %)		
Commercial	2,544	59%
Government	64	1%
Managed Medicaid	15	<1%
Medicaid	251	6%
Medicare	1,369	32%
Unknown	74	2%
Patient region of residence in the U.S. (n, %)		
Midwest	786	18%
Northeast	958	22%
South	1,190	28%
West	1,350	31%
Unknown	33	<1%

SD, standard deviation.

Cohort Treatment Patterns and Outcomes

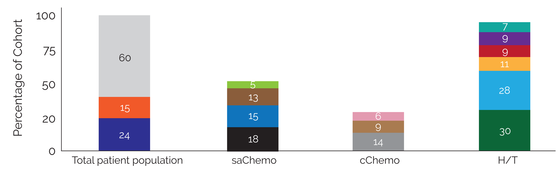
- The frequency of each treatment cohort in 1L was 61% hormonal or targeted therapy followed by cChemo (21%) and saChemo (18%).
- For all patients:
  - The median age for all patients initiated on 1L for H/T was 68 years, saChemo was 64 years, and cChemo was 61 years.
  - The most common regimens received in 1L by cohort were **(Figure 1)**:
    - H/T: anastrozole (25%), letrozole (23%), and fulvestrant (13%).
    - cChemo: cyclophosphamide plus doxorubicin (23%), cyclophosphamide and docetaxel (9%), and caboplatin and paclitaxel (4%).
    - saChemo: capecitabine (12%), paclitaxel (11%), and nab paclitaxel (11%).
- For patients identified with 2 or more comorbidities **(Figure 2)**:
  - Within each treatment cohort, cChemo had the least number of patients diagnosed with ≥2 comorbidities (5%) followed by saChemo and H/T (each were 7% respectively).
  - Approximately 61% received H/T, 15% cChemo, and 24% saChemo.
  - Among the respective treatment cohorts, eribulin was the most frequently used in the saChemo cohort (18%), cycolphosphamide plus doxorubicin in the cChemo cohort (14%), and anastrazole in the H/T cohort (30%).
  - Capecitabine was the most frequently received saChemo overall but was used to treat <5% of patients with ≥2 comorbidities.
- For patients diagnosed with visceral metastases **(Figure 3)**:
  - Within each treatment cohort, the greatest proportion of patients with diagnosed visceral meatastasis was saChemo (16%), followed by cChemo (14%), and H/T (12%).
  - Among all patients, the greated proportion of patients diagnosed with visceral metastases were treated with H/T (52%), followed by saChemo (28%), and cChemo (21%).
  - Among the respective treatment cohorts, the most frequently used saChemo were capecitabine (24%), cyclophosphamide plus doxorubicin in the cChemo cohort (13%), and anastrazole in the H/T cohort (25%).

Figure 1. Frequency of Regimens by Treatment Cohorts



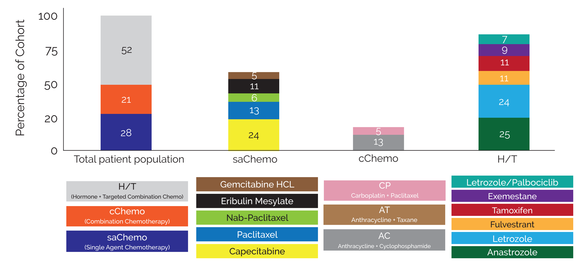
All regimens graphed were received in a frequency ≥5%.

Figure 2. Frequency of Regimens by Treatment Cohorts in Patients with ≥2 Comorbidities



All regimens graphed were received in a frequency ≥5%.

Figure 3. Frequency of Regimens by Treatment Cohorts in Patients with Visceral Metastases



All regimens graphed were received in a frequency ≥5%.

Disease Progression

- The proportion of patients on therapy at 6 months following drug initiation (based on Kaplan-Meier method) was:
  - saChemo: paclitaxel (94%)
  - cChemo carboplatin plus nab paclitaxel (86%)
  - H/T: letrozole plus palbociclib (89%)

LIMITATIONS

- Analyses based on claims data are limited by the lack of clinical details including stage, confirmed molecular subtype, and mortality; and as such, the severity of disease and its impact on time to next treatment was unable to be considered.
- There may have been misclassification of molecular subtype of patients, resulting in the characterization of subtype using the National Comprehensive Cancer Network (NCCN) Guideline recommendations for each subtype and matching that to the prescribing patterns of the study population.

CONCLUSIONS

- This study is the first to our knowledge to describe the treatment patterns of HR+/HER2- mBC patients following the approval of CDK 4/6 inhibitors.
- Although these data were not divided by year, the frequency of palbociclib use increased each successive year following its FDA approval in 2015.
- Contrary to the NCCN Guidelines, chemotherapy constitutes approximately 40% of 1L regimens since the approval of CDK 4/6 inhibitors.
  - Our estimate of 1L chemotherapy utilization is conservative; patients who only receive one line of chemotherapy were excluded from the analysis.
- cChemo continues to be utilized for these patients despite an increase in side effects with no significant efficacy benefit.

References

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