

Treatment Patterns and Health Resource Utilization in Patients with HR+/HER2- Locally Advanced or Metastatic Breast Cancer in Real World Setting in Taiwan

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Purpose

- Twenty-five percent of all newly diagnosed metastatic cancers among women in Taiwan are breast cancer, making it the most commonly diagnosed within women [1].
- The selection of treatment for locally advanced and metastatic breast cancer (advanced breast cancer; ABC) depends on the hormone receptor status, menopausal status, prior treatment and extent of the disease. Systemic treatments such as endocrine therapy (ET) and cytotoxic chemotherapy (ChT) remain mainstream treatment options for the management of advanced hormone receptor positive (HR+) disease.
- Advances in the understanding of molecular heterogeneity and gene expression analysis over the past two decades has led to development of novel agents (i.e. abemaciclib) targeting pathways associated with specific cancer subtypes and offering increased survival compared with nonspecific therapies.
- The purpose of this study was to understand the current treatment patterns, survival and health resource utilization (HRU) of women with ABC living in Taiwan.

Patients and Methods

- A chart review was conducted in 118 female patients meeting the inclusion criteria of: ≥20 years old with HR+/ human epidermal growth receptor-negative (HER2-) ABC (including recurrence or de novo cases) diagnosed between January 2015 and December 2017 in Taiwan.
- Anonymized data on patient characteristics, treatment patterns and survival was abstracted by 30 physicians across all three regions of Taiwan.
- Oncologists were asked to identify eligible patients from those meeting the inclusion/exclusion criteria, based on a randomly generated month of birth to avoid selection bias, and review those patients' charts to report anonymized patient-level information.
- The data abstraction form included questions on each subject's demographic characteristics, cancer directed treatments, supportive care treatments, and HRU.
- This was a non-comparative study; however, a sub-group of patients was examined in a post-hoc analysis in addition to the total subject population that included post-menopausal (PM) women with no prior systemic therapy in the advanced setting that partially reflected the MONARCH 3 (NCT02246621) clinical trial patient eligibility criteria.
- In addition, baseline characteristics were examined in two additional subgroups based on the presence of visceral disease (defined as presence of any visceral disease at diagnosis of ABC, including malignant neoplasms of lung, liver, adrenal, pleural, peritoneal involvement, and other) and use of ChT as first-line treatment post ABC diagnosis. Treatment patterns were also assessed by presence of visceral disease.
- Descriptive statistics were used to characterize the sample and treatment patterns overall and within patient subgroups. Rates and 95% confidence intervals (CI) for HRU were evaluated using Poisson models, which included an offset of patient follow-up time. Progression-free and overall survival, were assessed using Kaplan-Meier methods.

Results

Physician sample characteristics

- Out of the 30 physicians participating in the data abstraction, 19 were medical oncologists, while 11 were surgical oncologists/surgeons. The type of facility as the primary location of work of the physicians varied across local community hospitals (40.0%), metropolitan hospitals (36.7%), and academic medical centers (23.3%).
- Each region of Taiwan were represented in the physician sample, as follows: north of Taiwan 15 (50.0%); south of Taiwan 9 (30.0%) and central Taiwan 6 (20.0%).
- The mean (SD) time physicians had been practicing in ABC was 14.9 (6.91) years, and they reported treating a median (IQR) of 30 (20–40) ABC patients per month.

Patient sample characteristics

- The mean (SD) age of the 118 patients was 56.6 (11.66) years and ranged from 29 to 83 years. The majority of patients (54.1%) were not employed. Most patients (92.4%) were alive at time of data collection, while 9 patients were deceased.
- A total of 56 patients met the eligibility criteria for the subgroup of PM women with no prior systemic therapy in the advanced setting. This patient group was similar to the overall patient population in general, but appeared to be older, and had a tendency of presenting more hypertension and diabetes comorbidities.
- Of the 118 patients, 54 had visceral disease and 64 did not. Patients with visceral disease were slightly older, were more likely to have comorbidities including: hypertension, diabetes, arthritis, depression and hyperlipidemia, more likely to be PM, have a higher Eastern Cooperation Oncology Group (ECOG) score, and have a greater number of metastatic sites, compared to patients without visceral disease.
- Of the 118 patients, 72 received first-line ChT and 46 did not. Patients with first-line ChT use were slightly younger, less likely to have hypertension and heart disease, less likely to be PM, have a higher ECOG score, have shorter time from initial diagnosis to first metastasis, slightly more likely to have visceral disease, and more likely to have bone and bone marrow metastasis compared to patients without ChT use during first-line therapy.

Table 1: Patient characteristics

Characteristics	PM with no prior ABC treatment (N=56)	Visceral disease (N=54)	ChT (N=72)	All patients (N=118)
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Age (years) ^a				
Mean (SD)	63.0 (7.99)	58.0 (11.82)	54.6 (10.24)	56.6 (11.66)
Range	43–83	35–83	32–83	29–83

Other characteristics, n (%)				
Alive at time of data abstraction, n (%)	53 (94.6)	49 (90.7)	66 (91.7)	109 (92.4)
Not employed [student, retired, other]	37 (69.8)	33 (63.5)	38 (55.1)	60 (54.1)

Comorbidities ^{b, c} , n (%)				
Hypertension	26 (46.4)	24 (44.4)	23 (31.9)	44 (37.3)
Arthritis	5 (8.9)	6 (11.1)	3 (4.2)	8 (6.8)
Thyroid problem	1 (1.8)	3 (5.6)	5 (6.9)	6 (5.1)
Hyperlipidemia	6 (10.7)	7 (13.0)	7 (9.7)	11 (9.3)
Hypercholesterolemia	1 (1.8)	2 (3.7)	3 (4.2)	4 (3.4)
Diabetes	17 (30.4)	14 (25.9)	15 (20.8)	24 (20.3)
GI disorders or GERD	5 (8.9)	8 (14.8)	10 (13.9)	16 (13.6)
Heart Disease	5 (8.9)	5 (9.3)	4 (5.6)	12 (10.2)
Respiratory Disease	0 (0.0)	2 (3.7)	1 (1.4)	3 (2.5)
Depression	4 (7.1)	8 (14.8)	9 (12.5)	12 (10.2)
Other	13 (23.2)	15 (27.8)	27 (37.5)	39 (33.1)

Hormone receptor status ^c , n (%)				
ER+	55 (98.2)	53 (98.1)	71 (98.6)	116 (98.3)
PR+	46 (82.1)	46 (85.2)	57 (79.2)	98 (83.1)
Both ER+ and PR+	45 (80.4)	45 (83.3)	56 (77.8)	96 (81.4)

Characteristics	PM with no prior ABC treatment (N=56)	Visceral disease (N=54)	ChT (N=72)	All patients (N=118)
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ECOG score at time of ABC diagnosis, n (%)				
0	15 (26.8)	9 (16.7)	18 (25.0)	40 (33.9)
1	41 (73.2)	38 (70.4)	49 (68.1)	68 (57.6)
2+	0 (0.0)	7 (13.0)	5 (6.9)	10 (8.5)
PM at time of ABC diagnosis, n (%)	56 (100.0)	35 (64.8)	37 (51.4)	70 (59.3)

Number of metastatic sites (number of organs involved)				
Mean (SD)	1.5 (0.71)	1.7 (0.72)	1.5 (0.82)	1.5 (0.75)
Range	0–3	0–3	0–3	0–3
Brain metastasis, n (%)	0 (0.0)	4 (7.4)	6 (8.3)	10 (8.5)
Bone and bone marrow metastasis, n (%)	30 (53.6)	28 (51.9)	41 (56.9)	63 (53.4)
Any visceral disease, n (%)	28 (50.0)	54 (100.0)	34 (47.2)	54 (45.8)

ABC, locally advanced or metastatic breast cancer; ChT, chemotherapy; ECOG, Eastern Cooperation Oncology Group; PM, post-menopausal; SD, standard deviation.
^a Age is measured as at date of data collection.
^b Comorbidities were measured as at date of data collection or at death.
^c Percentages may add to more than 100% as patients may be counted in more than one category.

ABC treatment patterns

- Anti-cancer treatments since diagnosis of ABC included a variety of therapies, including hormonal therapy (93.2%), ChT (66.9%), other targeted and biologic therapies (22.9%), ovarian suppression (22.9%), ovarian ablation (8.5%), as well as other radiation (35.6%) and other surgery (18.6%).
- Most patients in the sample had 2 lines of systemic therapy regimens only since diagnosis of ABC (41.5%). Less than one-third of patients (30.5%) had 1 line only, 21.2% had 3 lines, 2.5% had 4 lines, and 4.2% had 5 or more lines of systemic therapy regimens since diagnosis of ABC.
- There were 67 different regimens in first-line treatment among the 118 patients in the overall sample. The sample had 42 different second-line therapies among 82 patients and 25 different third-line therapies among 33 patients.
- The most common first- and second-line systemic therapy group after diagnosis of ABC was ET-based (39.0% and 47.6%, respectively) or ET+ChT combinations (38.1% and 35.4%, respectively). The most common third-line therapy groups were ET-based (39.4%) or ChT combinations (27.3%) or ET+ChT combinations (27.3%).
- In PM patients, the most common first-and second-line treatments were both ET-based with the proportion of patients receiving them being 44.6% and 47.2%, respectively [Table 2].

Adverse events

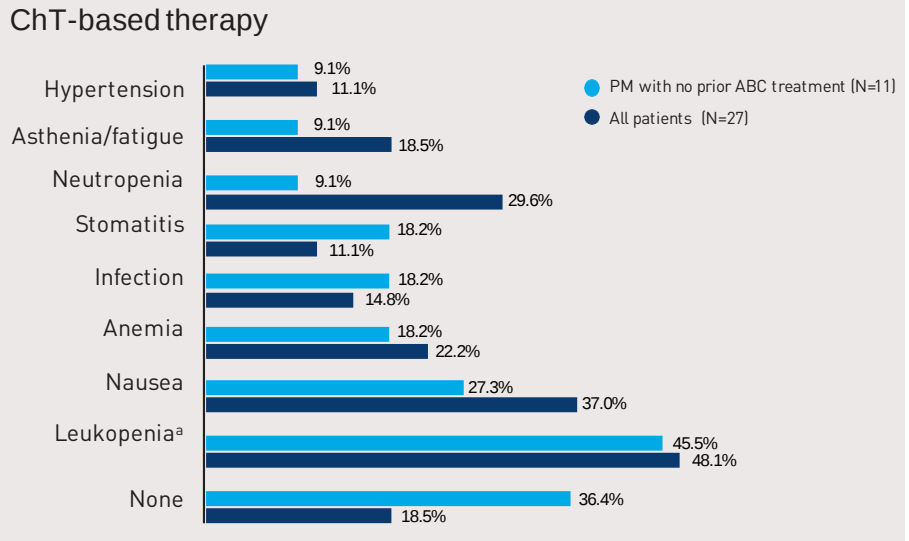
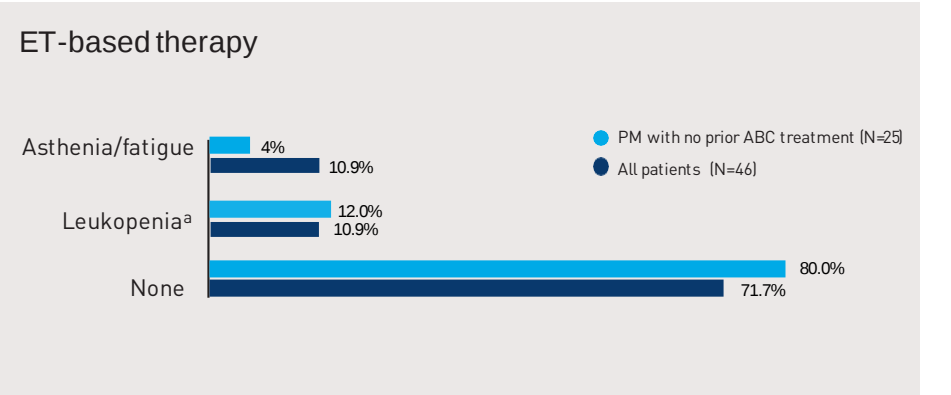
- The percentage of patients with ≥1 severe adverse event (≥grade 3) during first-line therapy was higher in patients on ChT-based regimen compared to ET-based (81.5% vs 28.3%).
- The most commonly reported severe adverse events (≥grade 3) during first-line were leukopenia (48.1%), nausea (37.0%), neutropenia (29.6%), and anemia (22.2%) for patients on a ChT-based regimen; and leukopenia (10.9%), and asthenia/fatigue (10.9%) for patients on ET-based therapy [Figure 1].

Table 2: Most common treatments (>10% of patients) after diagnosis of ABC

Treatment	PM with no prior ABC treatment (N=56)	Visceral disease (N=54)	All patients (N=118)
First-line therapy, n (%)			
ET-based	25 (44.6%)	20 (37.0)	46 (39.0)
ET monotherapy	18 (32.1%)	12 (22.2)	23 (19.5)
ET +/- ovarian suppression/ablation	3 (5.4%)	6 (11.1)	14 (11.9)
ET + targeted therapy ^a +/- ovarian suppression/ablation	4 (7.1%)	2 (3.7)	9 (7.6)
ET + ChT-based combinations	20 (35.7%)	20 (37.0)	45 (38.1)
ChT-based combinations	10 (17.9%)	13 (24.1)	25 (21.2)
Second-line therapy, n (%)			
ET-based	17 (47.2)	16 (39.0)	39 (47.6)
ET monotherapy	9 (25.0)	8 (19.5)	19 (23.2)
ET + targeted therapy ^a +/- ovarian suppression/ablation	6 (16.7)	6 (14.6)	11 (13.4)
ET +/- ovarian suppression/ablation	2 (5.6)	2 (4.9)	9 (11.0)
ET + ChT-based combinations	13 (36.1)	17 (41.5)	29 (35.4)
ChT combinations	5 (13.9)	5 (12.2)	9 (11.0)
Third-line therapy, n (%)			
ET-based	6 (46.2)	-	13 (39.4)
ET +/- targeted therapy ^a +/- ovarian suppression/ablation	4 (30.8)	-	9 (27.3)
ET monotherapy	2 (15.4)	-	4 (12.1)
ChT combinations	2 (15.4)	-	9 (27.3)
ET + ChT-based combinations	3 (23.1)	-	9 (27.3)

ABC, locally advanced or metastatic breast cancer; ChT, chemotherapy; ET, endocrine therapy; N, total number of patients having line of therapy; NA, not assessed; PM, post-menopausal.
^a Targeted therapy includes cyclin dependent kinase (CDK) inhibitors and mammalian target of rapamycin (mTOR) inhibitors.

Figure 1: Most common severe adverse events during 1st-line therapy (>10% of patients)



ABC, locally advanced or metastatic breast cancer; ChT, chemotherapy; ET, endocrine therapy; N, total number of patients having line of therapy; PM=post-menopausal;
Notes: Percentages may add to more than 100% as patients may be counted in more than one category; severe adverse event (≥grade 3).
^a Leukopenia was not necessarily reported separately if neutropenia or febrile neutropenia is also reported.

Health resource utilization

- Oncologist visits, at an average rate of 9.20 (8.81, 9.60) visits per person-year, and hospitalizations, with a rate of 1.08 (0.96, 1.22) per person-year, and a mean (SD) length of stay of 6.95 (6.71) days, were the key drivers of HRU.
- Among the diagnostic and disease monitoring tests, nearly all patients received chest X-ray, bone scan, tumor markers, and CT, while the majority of patients also received ultrasound, and about a third of patients received PET, and a quarter of patients received MRI.
- The annual rate of hospitalization was higher among the 72 patients who used ChT during first-line therapy compared to those who did not use ChT, 1.4 versus 0.45 admissions per person-year, respectively. However, the length of stay per hospitalization was shorter for patients who used ChT compared to those who did not, 6.1 days versus 11.4 days, respectively. Therefore, the overall number of days spent in hospital per person-year was approximately 8.5 and 5.1 days for patients who used ChT and those who did not use ChT, respectively.

Table 3: Health care resource utilization after diagnosis of ABC

	PM with no prior ABC treatment (N=56)	All patients (N=118)
Annual Rate [95% CI] ^a		

Diagnostic and monitoring tests		
Chest X-ray	1.31 (1.12, 1.53)	1.72 (1.57, 1.90)
CT	2.06 (1.82, 2.33)	1.86 (1.70, 2.04)
Tumor markers	3.15 (2.85, 3.49)	2.87 (2.67, 3.10)
Bone scan	1.23 (1.05, 1.45)	1.24 (1.11, 1.39)
Ultrasound	1.31 (1.13, 1.53)	1.76 (1.60, 1.94)
MRI	0.12 (0.07, 0.20)	0.23 (0.18, 0.30)
PET	0.20 (0.13, 0.29)	0.31 (0.24, 0.39)

Office Visits		
Oncologist	10.09 (9.53, 10.67)	9.20 (8.81, 9.60)
Surgeon	3.11 (2.81, 3.44)	3.94 (3.69, 4.20)
Pain or palliative physician	0.13 (0.08, 0.21)	0.31 (0.24, 0.39)
Other specialist physician	0.61 (0.48, 0.77)	0.85 (0.73, 0.98)
Accident and emergency visits	0.25 (0.17, 0.35)	0.31 (0.24, 0.39)
Hospitalization	0.70 (0.56, 0.86)	1.08 (0.96, 1.22)
Length of stay per hospitalization (days, SD)	8.46 (8.26)	6.95 (6.71)

ABC, locally advanced or metastatic breast cancer; CI, confidence interval; CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography; PM, post-menopausal; SD, standard deviation.

Discussion

- This study presents an up-to-date overview of current treatment patterns and HRU in patients with ABC in the real world setting in Taiwan. The sample provided a comprehensive geographic coverage of oncologists and surgical oncologists involved in treating ABC across Taiwan. Physicians in the sample had extensive knowledge of ABC with an average of over 14 years of experience in treating ABC patients.
- Results quantified a large burden of ABC in terms of treatments and HRU required, which were consistent with the severity of ABC. The findings also showed that treatment patterns in real world practice reflected clinical guidelines published internationally [2] in terms of systemic treatments such as ET and ChT options dominating ABC care with ovarian suppression with ET used in a certain portion of patients.
- Current treatment patterns suggest an unmet need for new medications, including for the overall patient population and the subgroups of patients based on PM status, presence of visceral disease, and first-line ChT use, that can lead to reduction in high rate of ChT use and frequent severe AEs associated with them.
- This unmet need was underlined with the finding that the prevalence of severe (≥grade 3) AEs during first-line systemic therapy after ABC diagnosis in real world setting was reported to be substantially higher in patients undergoing ChT treatment compared to ET-based treatments. In addition, HRU in terms of annual hospital admissions and overall number of hospital days was also substantially higher in ChT patients. Patients with ChT use may have more aggressive disease, as indicated by a higher ECOG score and presence of visceral disease.
- The results also highlighted factors associated with the use of ChT as first-line therapy, including younger age, less likelihood of hypertension and heart disease (potentially due to being younger), less likelihood of being PM, higher ECOG score, and more likelihood of visceral disease and bone and bone marrow metastasis, compared to those without ChT as first-line therapy.
- Some limitations of this study need to be highlighted. Patients who already died at the time of data collection may have been underrepresented in the sample, and, as such, overall survival estimates were not possible to accurately estimate.
- Results of this study can inform future health economic evaluations of new ABC treatments that estimate the cost-effectiveness or budgetary impact of adopting them in Taiwan.

References

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