Healthcare resource utilization for first line chemotherapy versus endocrine therapy in patients with advanced HR-positive/HER2-negative breast cancer in Taiwan

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Abstract

Objective

The goal of this retrospective database analysis was to describe treatment patterns, compare healthcare resource utilization, and evaluate frequency of potential treatment-related toxicity among patients with hormone receptor-positive (HR+) and human epidermal growth factor receptor 2-negative (HER2–) advanced breast cancer using upfront endocrine therapy or chemotherapy, as well as to assess the effect of choice of systemic treatment on survival outcome in Taiwan.

Methods

Eligible HR+ HER2– advanced breast cancer patients were identified using Taiwan Cancer Registry from 2011-2017 and Taiwan National Health Insurance database from 2011-2018 and classified as those who received first line chemotherapy or endocrine therapy. Comparisons between these two groups were made in terms of number of hospitalization episodes, hospitalization duration, healthcare resource utilization and frequency of potential treatment-related toxicity. Survival outcomes were evaluated by Kaplan-Meier method.

Results

There were 2,874 patients with HR+ HER2– advanced breast cancer during the study period, 42% of them received first line endocrine therapy and 56% received first line chemotherapy. Mean hospitalization episodes were higher in the first line chemotherapy group compared to first line endocrine therapy in the first year after initial breast cancer diagnosis, and the number of hospitalization episodes were similar in the second and third year. Treatment for adverse events likely to be associated with cancer treatment, such as blood transfusion, emergency department visits, use of granulocyte-stimulating colony factor, anti-inflammatory medication and intravenous antibiotics were more commonly administered in patients who received chemotherapy as initial therapy. Multiple regression analysis showed that first line chemotherapy as initial therapy was associated with higher level of healthcare resource utilization in the first year compared to first line endocrine therapy but the differences were not statistically significant in the second and third year. Use of chemotherapy or endocrine therapy were associated with similar survival outcomes over three years.

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Conclusion

In Taiwan, a higher percentage of patients with HR+ HER2– advanced breast cancer were started on chemotherapy in the recent decade, more frequent hospitalizations and higher incidence of adverse events were associated with the use of chemotherapy, and they had higher healthcare resource utilization than those who were prescribed endocrine therapy. Data from this analysis can help inform optimal management of advanced breast cancer.

[Keywords] Taiwan National Health Insurance database, HR+ HER2– advanced breast cancer, chemotherapy, endocrine therapy, healthcare resource utilization

Introduction

According to the latest GLOBOCAN 2018 statistics, breast cancer was the most common cancer in females globally as well as in East Asia [1]. Modern cancer treatments are expensive; in Taiwan, cancer expenditure accounted for 10.2% of National Health Insurance (NHI) total expenditure in 2012 [2]. Throughout the years, incidence of breast cancer has been increasing steadily, which contributed to the increasing expenditure borne by the NHI [3]. With escalating healthcare expenditure in Taiwan, there is a need to optimize cancer treatment to maintain long term sustainability of NHI.

Current international treatment guidelines recommend that endocrine-based therapy be the preferred first line strategy for hormone receptor positive (HR+) human epidermal growth factor receptor 2-negative (HER2–) advanced breast cancer, while chemotherapy is deferred unless there is visceral crisis or endocrine treatment resistance [4, 5]. However, in real-world practice, first line chemotherapy is still used extensively in Europe and United States [6].

To our knowledge there are limited publications on healthcare resource utilization of endocrine therapy and chemotherapy in patients with HR+ HER2– advanced breast cancer in Taiwan to date. In this population-based study in Taiwan we described treatment patterns for HR+ HER2– advanced breast cancer (*de novo* stage 4) and compared healthcare resource utilization, frequency of potential treatment-related toxicity and survival between those who received upfront chemotherapy or endocrine therapy.

Methods

We carried out a retrospective cohort study utilizing secondary health data in Taiwan.

Data source

Taiwan launched the National Health Insurance program in 1995, which covers up to 99% of the population. Insurance claims data for ambulatory visits, emergency service, hospital care and drug prescriptions are included in the NHI data [7]. In addition, the Taiwan Cancer Registry was established to collect information on all newly diagnosed cancer cases from hospitals with 50 or more beds, and it has cancer staging and histology information; as well as tumor marker data for selected cancer [8]. The Department of Statistics at Taiwan Ministry of Health and Welfare maintains a repository of health data for public health research, including the NHI, Taiwan Cancer Registry, and mortality statistics, which are linkable through the encrypted and unique national identifier for each individual. This study was approved by the National Taiwan University Hospital Research Ethics Committee (case number 201905085RINA). Individual informed consent was waived because of the use of de-identified data.

Study population

We identified all patients age 20 or older who had a first breast cancer diagnosis (International Classification of

Diseases, 9th revision, Clinical Modification [ICD-9-CM] code 174-175, or ICD-10-CM code C50.0-C50.9) from 2011 through 2017 from Taiwan Cancer Registry and restricted the study population to those who had *de novo* stage 4 disease per American Joint Committee on Cancer (AJCC) staging, 7th edition [9]. The *de novo* stage 4 breast cancer population was further evaluated according to the "Site Specific Factor (SSF)" data field in the Cancer Registry and cancer treatment information from NHI. From 2011 onward, ER status and HER2 status were recorded in Taiwan Cancer Registry in the SSF data field for breast cancer patients, and the HR+ HER2– target population could be defined accordingly. In addition, we utilized drug use information in NHI to exclude patients whose treatment regimens were not compatible with HR+ HER2– advanced breast cancer. Those who had ever received trastuzumab, a standard of care for HER2+ subtype and those who received treatment for stage 0, 1, or 2 breast cancer or for local recurrence of breast cancer were excluded.

NHI and national mortality statistics data from 2011 through 2018 were utilized so that all patients would have at least one year of post-diagnosis follow-up. All patients were followed for up to three years after the breast cancer diagnosis.

Outcomes of interest

Treatment category was defined by the first systemic treatment after breast cancer diagnosis and further classified by record of surgery. The hospital level that a patient received the most treatment regimen during the first year after initial diagnosis was classified as medical center, regional hospital, or could not be classified. A patient could receive endocrine therapy (ET) only, chemotherapy (CT) only or both. Those who received concomitant ET + CT were included in the CT group unless the patient only received low dose oral cyclophosphamide, who would be categorized under ET as initial therapy. Only surgeries directed at the primary breast tumor during the first year after initial diagnosis were identified, including but not limited to partial mastectomy, mastectomy, modified radical mastectomy, and any type of lymph node dissections. Other cancer-related surgeries, such as central venous port insertion or bone surgery for fracture were not included. As we were unable to differentiate the type of radiation and to which site it was applied because of the NHI coding system, radiation therapy to all anatomical sites were identified. We identified all hospitalization episodes and duration of hospital stay. The type of hospital (medical center or regional hospital) that a patient received cancer treatment was defined according to the one with the most visits during the first year after initial diagnosis. NHI reimbursement amount for each treatment item (ET, CT, surgery, and radiation therapy) were identified.

We assessed treatment for common toxicities associated with systemic treatment, include nausea/vomiting, mucositis, myelosuppression and serious infections (represented by intravenous antibiotics). Psychiatry visits and treatment for mental health conditions were also evaluated.

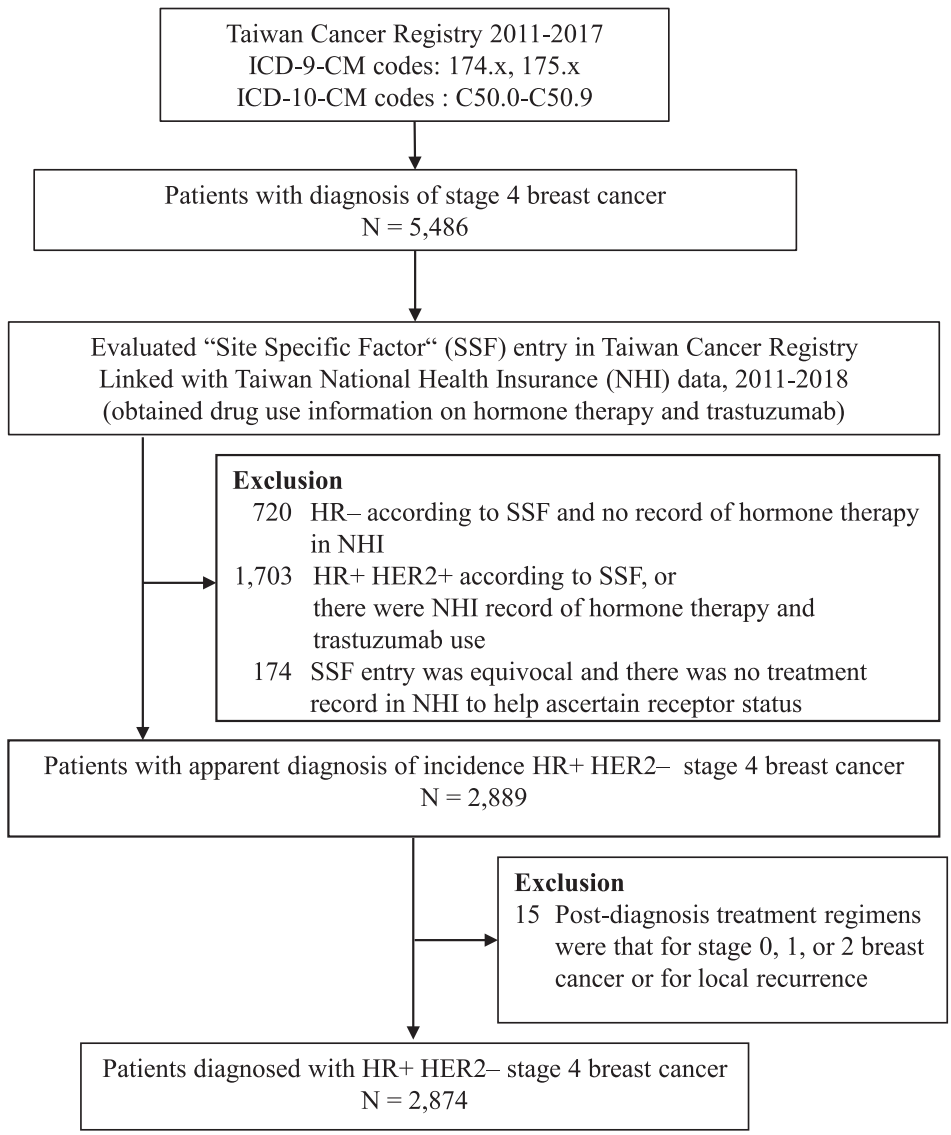
Statistical analysis

Data were presented descriptively with appropriate metrics (proportion, mean and standard deviation [SD], or median). Comparative analysis was restricted to patients who received ET or CT. Healthcare resource utilization costs were presented in US Dollar under the assumption of an exchange rate of 1 US dollar to 30 Taiwan dollar. Multiple linear regression was used to evaluate the effects of treatment modality (ET or CT) on healthcare resource utilization in each of the three years during follow-up while controlling for patients' age, level of hospital, breast surgery and radiotherapy during the first year after initial diagnosis. Chi square test was used to compare proportions of patients who received treatment for adverse outcomes association with breast cancer treatment between the ET and CT groups. Three-year survival outcomes between the two treatment groups were described using Kaplan-Meier method.

Results

Baseline characteristics

A total of 2,874 patients were identified from Taiwan Cancer Registry as having incident *de novo* Stage 4 HR+ HER2– advanced breast cancer from 2011 through 2017 (Figure 1). A majority of them were female (99.5%). Mean age of patients at initial diagnosis was 57.9 (SD 13.0) (Table 1).



Abbreviations: ICD-9/10-CM, International Classification of Diseases, 9th/10th Revision, Clinical Modification; HER2, Human Epidermal Growth Factor 2; HR, Hormone Receptor; NHI, National Health Insurance; SSF, Site Specific Factor

Figure 1. Identification of study subjects

Table 1. Baseline demographics of patients diagnosed with de novo Stage 4 HR+ HER2– breast cancer in Taiwan, 2011-2017

	Stage 4 HR+/HER2- Breast Cancer
N	2,874
Gender, n (%)	
Male	15 (0.5)
Female	2,859 (99.5)
Age, mean (SD)	57.9 (13.0)
Age group, n (%)	
20-39	182 (6.3)
40-49	618 (21.5)
50-59	851 (29.6)
60-69	686 (23.9)
≥ 70	537 (18.7)

Treatment patterns and healthcare resource utilization

More than half (1,627 out of 2,874, 56.6%) of the advanced breast cancer patients received treatment at a medical center during the year after initial diagnosis and about 40% (1,142 out of 2,874) received treatment at a regional hospital. All but 44 of them had records of treatment after the initial diagnosis and the vast majority of them (98%) received systemic treatments. (Table 2) A total of 1,207 patients (42%) received first line ET and 1,610 patients (56%) received first line CT. Among patients whom we classified as receiving CT as initial treatment,

Table 2. Treatment patterns among 2,874 patients with HR+ HER2– advanced breast cancer

	Total	Level of hospital that provided the treatments		
		Medical Center	Regional Hospital	Other or unclassified
	n (%)	n (%)	n (%)	n (%)
Total patients	2,874	1,627	1,142	105
First line ET	1,207 (42.0)	696 (42.8)	460 (40.3)	51 (48.6)
ET without breast surgery	544 (18.9)	336 (20.7)	181 (15.8)	27 (25.7)
ET with breast surgery	169 (5.9)	105 (6.5)	58 (5.1)	6 (5.7)
ET + CT without breast surgery	321 (11.2)	169 (10.4)	141 (12.3)	11 (10.5)
ET + CT with surgery	173 (6.0)	86 (5.3)	80 (7.0)	7 (6.7)
Switch to CT or added CT to treatment regimen in first year†	494 (40.9%)	-	-	-
First line CT	1,610 (56.0)	904 (55.6)	667 (58.4)	39 (37.1)
CT without breast surgery	590 (20.5)	345 (21.2)	227 (19.9)	18 (17.1)
CT with breast surgery	703 (24.5)	391 (24.0)	301 (26.4)	11 (10.5)
CT + ET without breast surgery	238 (8.3)	126 (7.7)	112*	
CT + ET with breast surgery	79 (2.7)	42 (2.6)	37*	
Switched to ET or added ET to the regimen in first year‡	317 (19.7%)	-	-	-
Without systemic treatment	57 (2.0)	27 (1.7)	15 (1.3)	15 (14.3)
Breast surgery or Radiotherapy	13 (0.5)	6 (0.4)	7 (0.6)	0 (0.0)
No record of treatment	44 (1.5)	21 (1.3)	8 (0.7)	15 (14.3)

†Percentage is based on total number of patients on first line ET ‡Percentage is based on total number of patients on first line CT *Cell size of 3 or less in a table could not be individually presented and the table cells were combined
Abbreviations: ET, endocrine therapy; CT, chemotherapy

317 patients received CT plus ET combination. Overall, nearly 40% of patients (n=1,124) had received breast surgery in the first year after diagnosis, 342 patients in the first line ET group and 782 patients in the first line CT group. During the first year after diagnosis, 494 (40.9%) of patients on initial ET had either switched to CT or had CT added to the regimen, while 317 (20%) patients on initial CT switched to ER or had ET added to the regimen (Table 2).

Further analysis was restricted to the 2,817 patients who received systemic treatment. The mean number of hospitalization events were similar across patients who were prescribed first line ET from the first year to third year of diagnosis while patients on first line CT had a higher mean number of hospitalization episodes in the first year (5.8 and 6.3 hospitalization episodes, without breast surgery and with breast surgery, respectively) (Table 3). Except the first year in which there was an apparent difference in number of hospitalization episodes, the number of hospitalization episodes and length of hospital stay, regardless of underlying cause of hospitalization, were generally similar between the ET and CT groups (Table 3).

Median NHI reimbursement amount for treatment among the first line CT group was apparently higher than that among the first line ET group. When taking breast surgery into consideration, patients who had received surgery in addition to either first line CT or ET had larger reimbursement amount in the first year compared to those who had not. Patients who received surgery seemed to have lower cost in the second and third year, and the trend was more conspicuous in the group that received first line CT (Table 3).

Table 3. Healthcare resource utilization among 2,817 HR+ HER2- advanced breast cancer patients*

	First line ET (N=1,207)		First line CT (N=1,610)	
	Without breast surgery (N=865)	With breast surgery (N=342)	Without breast surgery (N=828)	With breast surgery (N=782)
Mean number of hospitalization episodes (SD)				
Year 1	3.3 (3.1)	3.6 (3.4)	5.8 (4.6)	6.3 (5.3)
Year 2	3.1 (3.3)	2.6 (2.3)	3.8 (3.6)	3.7 (3.6)
Year 3	3.3 (3.7)	3.2 (3.4)	3.7 (3.8)	3.7 (5.2)
Median duration of hospitalization stay (days)				
Year 1	19	12	26	16
Year 2	12.5	9	14	13
Year 3	11	14	15	14
Median NHI reimbursement amount associated with treatment, US dollar				
Year 1	10,641	14,847	18,110	21,084
Year 2	6,995	6,145	10,018	6,463
Year 3	6,238	5,784	9,803	6,103

*As a result of cancer deaths and follow-up cut-off at 2018, not all patients had three years of follow-up
Abbreviation: ET, endocrine therapy; CT, chemotherapy; NHI, National Health Insurance

Multiple linear regression was used to estimate the differences in healthcare utilization costs between ET and CT while adjusting for patients' age, breast surgery and radiotherapy in the first year, and level of hospital care for each of the three years after initial breast cancer diagnosis First line CT was associated with a significantly higher costs in the first year compared to first line ET ($p < 0.0001$), but the differences were not statistically significant in the second and third year. Breast surgery in the first year was associated with higher costs in the first year ($p=0.0051$) and was associated with lower costs in the second and third year ($p < 0.0001$ and 0.0002). Older age at diagnosis was associated with lower costs in general (Table 4).

Table 4. Multiple linear regression on the effect of systemic treatment modalities for HR+ HER2– advanced breast cancer on healthcare resource utilization

	Estimate (in US Dollar)	95% confidence interval		p-value
First Year				
Initial treatment (CT vs. ET)	4,883	4,212	5,554	<0.0001
Age at diagnosis (per year)	-78	-103	-52	<0.0001
Regional hospital vs. Medical center	-662	-1,296	-28	0.0408
Breast surgery vs. no surgery	953	286	1,620	0.0051
Radiotherapy vs. no radiotherapy	7,200	6,545	7,855	<0.0001
Second Year				
Initial treatment (CT vs. ET)	327	-449	1,102	0.4091
Age at diagnosis (per year)	-65	-94	-36	<0.0001
Regional hospital vs. Medical center	-299	-1,029	431	0.4222
Breast surgery vs. no surgery	-1,943	-2,684	-1,201	<0.0001
Radiotherapy vs. no radiotherapy	8,897	8,011	9,784	<0.0001
Third Year				
Initial treatment (CT vs. ET)	683	-440	1805	0.2330
Age at diagnosis	-49	-92	-5	0.0274
Regional hospital vs. Medical center	131	-924	1186	0.8080
Breast surgery vs. no surgery	-2,031	-3,094	-969	0.0002
Radiotherapy vs. no radiotherapy	10,160	8,792	11,528	<0.0001

Abbreviation: CT, chemotherapy; ET, endocrine therapy

As for management of treatment-related adverse effects, within the first year after initial diagnosis, compared to those who received first line ET, patients who were prescribed first line CT required more platelet transfusions (7.3% vs 5.6%) or blood transfusions (37.5% vs 30.5%), granulocyte-colony stimulating factor use (46.0% vs 14.1%), antiemetics (96.3% vs 66.3%), intravenous antibiotics (73.4% vs 57.8%), steroid oral paste (28.9% vs 19.0%), and mycostatin oral suspensions (5.9% vs 2.9%). There was also a higher percentage of anti-hepatitis B virus drugs prescribed in the first line CT group as expected, due to the use being mandated by practice guidelines in Taiwan for patients undergoing chemotherapy (Table 5).

Table 5. Management of treatment-related toxicities among 2,817 HR+ HER2– advanced breast cancer within one year after initial diagnosis

	ET as initial treatment N=1,207	CT as initial treatment N=1,610	p-value
CT-related regimen, n (%)			
Cardiac ultrasound (pre-CT use)	379 (31.4)	616 (38.3)	0.0002
Antiemetics prophylaxis for CT	800 (66.3)	1,551 (96.3)	<0.0001
Antiviral agent for hepatitis B (related to CT)	65 (5.4)	182 (11.3)	<0.0001
Anti-inflammatory medication, n (%)			
Steroid injection	625 (51.8)	1,504 (93.4)	<0.0001
Steroid oral base	459 (38.0)	999 (62.0)	<0.0001
Steroid oral paste	229 (19.0)	465 (28.9)	<0.0001
Pain medications, n (%)			
Non-steroidal anti-inflammatory drug	884 (73.2)	1,304 (81.0)	<0.0001
Opioid	861 (71.3)	1,203 (74.7)	0.0444
For mental health conditions, n (%)			
Outpatient psychiatry visits	107 (8.9)	132 (8.2)	0.5300
Antidepressant	181 (15.0)	250 (15.5)	0.6979
Anxiolytic agent	626 (51.9)	996 (61.9)	<0.0001
Hypnotics agent	354 (29.3)	576 (35.8)	0.0003
Barbiturates	0 (0.0)	0 (0.0)	
Short-acting benzodiazepine	111 (9.2)	176 (10.9)	0.1319
Intermediate-acting benzodiazepine	169 (14.0)	277 (17.2)	0.0212
Long-acting benzodiazepine		7	0.2503
Non-benzodiazepine hypnotics*	188 (15.6)	303 (18.8)	0.0247
Management of adverse events, n (%)			
Platelet transfusion	67 (5.6)	118 (7.3)	0.0594
Blood transfusion (with platelet)	368 (30.5)	603 (37.5)	0.0001
Intravenous fluid/nutrition supply	973 (80.6)	1527 (94.8)	<0.0001
Emergency room visits	614 (50.9)	883 (54.8)	0.0364
Drugs for adverse events, n (%)			
Granulocyte colony-stimulating factor	170 (14.1)	741 (46.0)	<0.0001
Intravenous antibiotics (excluding use for surgical prophylaxis)	698 (57.8)	1182 (73.4)	<0.0001
Antimycotics	36 (3.0)	51 (3.2)	0.7787
Mycostatin (Oral use)	35 (2.9)	95 (5.9)	0.0002

* Non-benzodiazepine hypnotics include zopiclone, eszopiclone, zaleplon and zolpidem.
Abbreviations: CT, chemotherapy; ET, endocrine therapy

Survival outcomes

Three-year survival outcome among the ER and CT groups are shown in Figure 2, which were generally the same for either ET or CT as initial therapy with the curve converging from year 2 onwards.

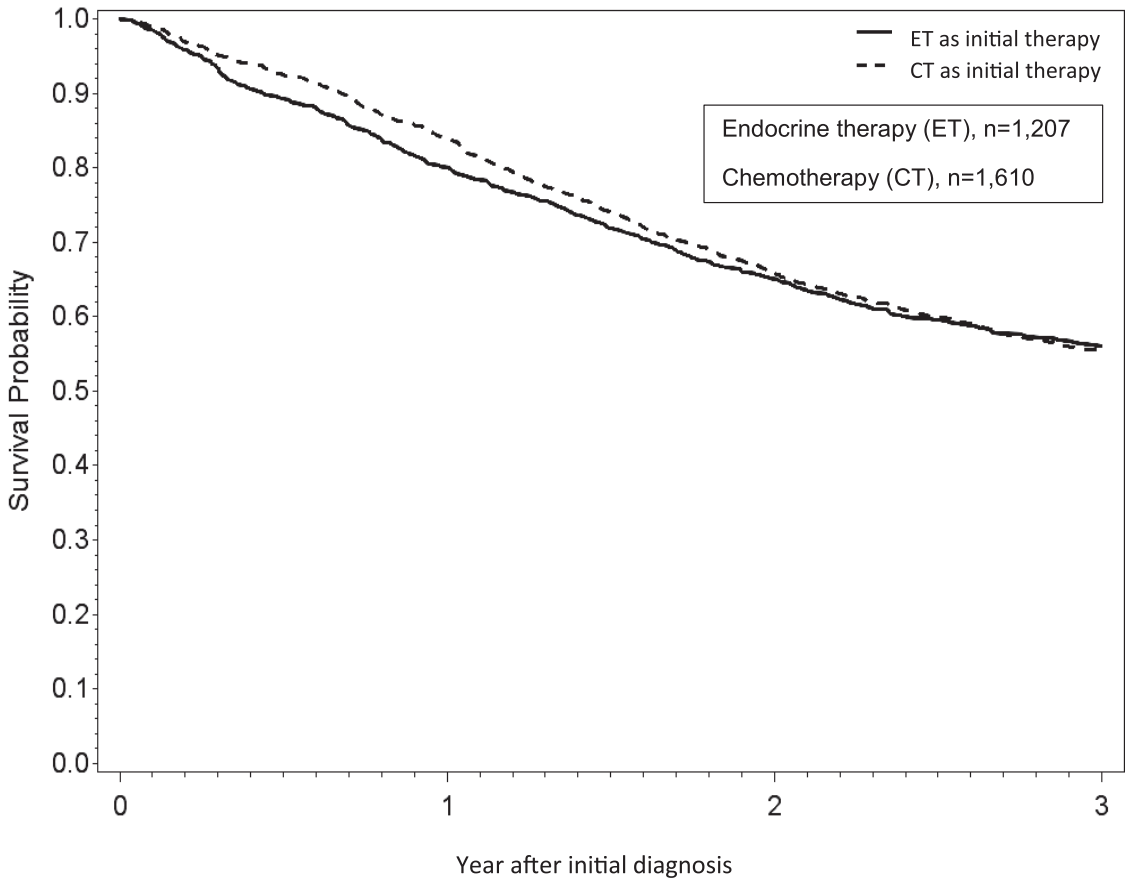


Figure 2. Survival among HR+ HER2- advanced breast cancer patients over three years after initial diagnosis in Taiwan

Discussion

To the best of our knowledge, this is the first population-based report on first line systemic treatment strategy for HR+ HER2– stage 4 breast cancer in Taiwan. Its strength is the population-based nature of the data source, such that we could identify all eligible patients during the study period from Taiwan. More patients received CT (56%) than ET (42%) as the first line therapy. There was a relatively high rate of surgery (39.1%) among these patients, which was inconsistent with treatment guidelines. Use of first line CT was generally associated with higher cost of treatment compared to first line ET, especially in the first year (USD18,110 vs USD10,641). These findings are similar to that reported for treatment costs for advanced breast cancer in US, Canada and Europe [10-13]. Unsurprisingly, the addition of breast surgery to systemic therapy increases the cost in the first year of diagnosis, however the cost in the subsequent years are lower than those that did not receive surgery. This could be due to

the different regimens used versus primary chemotherapy protocols which may affect costs, as well as possibly reduced adverse events.

The three-year survival was similar in either ET first or CT first group, which is consistent with that of a US study, where first-line CT was not associated with a survival benefit, but had significantly higher costs compared with first line ET[14]. Although the overall percentage of initial CT was high and seemed not adhering to current treatment guidelines, we observed a trend of increasing utilization of ET first strategy over the years: from 30% in 2011 to 49% in 2017 (data not shown).

In Taiwan, most CTs are delivered in hospitals, resulting in higher cost, and delivery of CT in out-patient clinics was not common until recent years. CT is usually associated with more side effects compared to ET, such as nausea, vomiting and diarrhea, while hot flashes being more common with endocrine therapy [15]. Prophylaxis antiemetics are prescribed as standard of care to prevent chemotherapy-induced nausea and vomiting, as evidenced by the data. A certain proportion of patients on ET were also prescribed antiemetics which may be attributed to the use of low potency anti-emetics, such as dopamine agonists, and the fact that 41% of patients had added or switched to CT within the first year. CT is also associated with increased risk of infections due to myelosuppression [16]. Granulocyte-stimulating colony factors are also usually prescribed alongside CT to treat or to prevent neutropenia [17], but not indicated for ET of which neutropenia is not a known side effect [18]. However, under NHI, use of granulocyte-stimulating colony factors is only reimbursed for the treatment of neutropenic sepsis or grade 4 neutropenia, not for prophylaxis. Therefore, the actual cost should be higher as some patients would have paid for granulocyte-stimulating colony factors out-of-pocket. Consequences of myelosuppression was also reflected by the higher rate of platelet, blood transfusion, and intravenous therapeutic antibiotics for patients on CT.

Generally, a diagnosis of breast cancer is associated with a deterioration of mental well-being with a reported prevalence of 0-58% [19]. The psychosocial stress is especially high for incurable stage 4 disease. Intriguingly, ETs are well known to be associated with the adverse effects as insomnia and depression [20, 21]. In our study, patients on first-line CT were prescribed with more anxiolytics and hypnotic agents than those on ET, although frequency of psychiatric consultation was similar between two groups. These findings suggested that in Taiwan side effects of chemotherapy resulted in more discomfort than the pharmacologic effect of endocrine therapies and compromised quality of life, which in turn contributed to a higher level of healthcare expense and burden. Furthermore, the more frequent hospital visits, admission, and intravenous injections accompanying chemotherapy further burdened the patients.

As a population-based study, we did not exclude men, although the small number of male patients did not allow us to draw inference from this subgroup. Interestingly, we observed that older patients had lower medical cost utilization compared with younger patients. It is probable that older patients may be more frail and treating physicians tend to apply dose modifications when prescribing chemotherapies and use less combination chemotherapies; once neutropenia occurs, the treating physician would tend to lengthen the treatment interval rather than using granulocyte-stimulating colony factors to meet chemotherapy schedules.

As a study based on secondary health data, a limitation of our study was that no additional clinical information was available for individual patients. The clinical condition of the patients would dictate which therapy was recommended, e.g. if a patient was in visceral crisis or had aggressive disease, chemotherapy would the recommended therapy. Usually, it would be assumed that patients who received endocrine therapy do not have serious disease burden. However, for certain fragile patients, endocrine therapy is the only option regardless of disease extent due to poor tolerance to chemotherapy.

This study was conducted before cyclin-dependent kinase 4 and 6 (CDK 4/6) inhibitors use was approved and reimbursable under NHI, as CDK4/6 inhibitors were only approved for reimbursement from October 2019. The benefit of adding CDK4/6 inhibitors to endocrine therapy has been consistently proven in clinical trials, with ribociclib, palbociclib and abemaciclib prolonging progression free survival [22-25] and as well as ribociclib significantly improving overall survival in advanced breast cancer [26]. The impact of CDK4/6 inhibitors is transforming management of breast cancer, and nowadays, the combination of CDK4/6 inhibitors and endocrine therapy has become the first line standard of care. Although CDK4/6 inhibitors are generally more expensive, CDK 4/6

inhibitors are usually very well tolerated along with the added survival benefits. More studies are required to understand the healthcare resource utilization comparison of CDK4/6 inhibitors compared with other therapies.

Conclusion

Our analysis of healthcare costs associated with treating HR+ HER2– advanced breast cancer using data from the Taiwan NHI has provided a snapshot on the population-based impact in Taiwan and we showed that healthcare resource utilization was higher in patients prescribed chemotherapy compared to endocrine therapy, as well as the higher level of toxicity associated with treatment. Three-year survival analysis showed that mortality outcomes were similar between first line CT and ET, which is supportive of the current international consensus to consider ET first. The treatment landscape has changed and the combination of CDK4/6 inhibitors and ET have now become the standard of care. Findings from this analysis would help inform future healthcare resources planning in management of advanced breast cancer.

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