Treatment patterns in HER2+/HR+ postmenopausal women with metastatic breast cancer initiating first-line treatment in a community oncology setting in the US

Puza P. Sharma, MD, PhD,[1] Kavita Sail, PhD,[2] Thomas E. Delea, MSIA,[3] and Debra A. Patt, MD, MPH[2]

[1] GlaxoSmithKline, Philadelphia, Pennsylvania; [2] Mckesson Specialty Health and The US Oncology Network, Houston, Texas; [3] Policy Analysis Inc, Brookline, Massachusetts

Background Within community oncology practices, the regimens used for treatment of postmenopausal women with human epidermal growth factor receptor 2- and hormone receptor-positive metastatic breast cancer (MBC) may vary.

Objective A retrospective observational study was conducted to examine treatment patterns in HER2+/HR+ patients initiating first-line treatment in a community oncology setting.

Methods Using US Oncology's iKnowMed electronic health records (EHRs), postmenopausal HER2+/HR+ patients who had been newly diagnosed with MBC between January 1, 2007 and June 30, 2010 were identified and stratified by visceral crisis.

Results We identified 347 postmenopausal HER2+/HR+ patients, of whom 258 (74%) did not have evidence of visceral crisis. Chemotherapy plus targeted plus hormone therapy was the most frequently used treatment strategy (33%). Trastuzumab was the most frequently used HER2 targeted therapy (77% and 66% with and without visceral crisis, respectively); followed by lapatinib. Paclitaxel (24%, nonvisceral; 39% visceral) and letrozole (26%, nonvisceral; 28% visceral) were the most frequently used chemotherapy and endocrine therapies, respectively. Over time, trastuzumab use decreased whereas lapatinib use increased.

Limitation The heterogeneity in the regimens prescribed precluded large sample sizes for robust statistical analyses to link specific therapeutic combinations with outcomes.

Conclusion Community oncologists use a variety of treatments in postmenopausal women with HER2+/HR+ MBC. Although a combination of chemotherapy, targeted HER2 therapy, and hormone therapy were the most common first-line therapies used, contrary to treatment guidelines, a large proportion of patients received no chemotherapy in the first-line setting.

Breast cancer is the most common malignancy in the United States, second only to lung cancer as a cause of cancer-related death.[1,2] Treatment choices in metastatic breast cancer (MBC) are dependent on both patient and tumor characteristics. Patient characteristics that guide treatment selection include age, comorbid illness, performance status, and patient preference. Pathologic characteristics that influence treatment decisions include the stage of disease, grade of the tumor, presence of genetic mutations, burden of disease, location of metastasis, presence of visceral crisis, as well as human epidermal growth factor receptor 2 (HER2) and hormone receptor (HR) status. About half of the breast cancers that overexpress HER2 also express HRs.[3,4] Preclinical and clinical data suggest that HER2 overexpression confers intrinsic resistance to hormone therapy and is an independent adverse prognostic factor regardless of the hormonal status of the tumor.[5,6]

Manuscript received August 2, 2012; accepted November 16, 2012.

Correspondence Debra A. Patt, MD, MPH, US Oncology, 6204 Balcones, Austin, TX 78731 (Debra.Patt@USONCOLOGY.com).

Disclosures The authors have no disclosures. The research was supported by GlaxoSmithKline.

Commun Oncol 2013;10:74-81

There is no consensus treatment algorithm for patients with HER2+/HR+ MBC. In particular, there is considerable uncertainty regarding the appropriate use of sequential single agents versus chemotherapy combinations and how patients' prognostic factors, such as visceral crisis and performance status, affect treatment received. Although traditionally HER2+ cancers have been treated with chemotherapy and targeted therapy, there is evidence on the efficacy of combined anti-HER2 and hormone therapy in the subgroup of patients with HER2+/HR+ breast tumors. The TrAstuzumab in Dual HER2 ER positive Metastatic breast cancer (TAnDEM) study was a large multicenter phase 2/3 trial that examined the benefit of adding trastuzumab to an aromatase inhibitor.[7] Results from the trial indicated a significant improvement in progression-free survival (4.8 months vs 2.4 months); overall response rate (20.3% vs 6.8%); and trend toward prolonged overall survival (28.5 months vs 23.9 months), with combined treatment as opposed to hormone treatment alone.

Other clinical studies have also indicated a progression free survival advantage by adding trastuzumab or lapatinib to aromatase inhibitors in postmenopausal women with HR-positive MBC.[8-10] For example, in postmenopausal women with MBC who coexpress HR and HER2, lapatinib-letrozole combination versus letrozole alone is associated with a significantly lower risk for disease progression (progression free survival, 8.2 vs 3.0 months, respectively), higher overall response rate (28% vs 15%), and clinical benefit rate (48% vs 29%).[11,12] Lapatinib plus letrozole is currently indicated as first-line therapy for HER2+/HR+ MBC in postmenopausal women. Trials have also established evidence regarding efficacy of combined anti HER2 targeted therapy with chemotherapy.[13-19]

Despite these advances and guidelines, the prescribing pattern for first-line therapy of HER2+/HR+ patients with MBC in the community oncology practice is not known. Furthermore, it is not known whether the prescribing patterns differ depending on patients' performance status and whether or not they have visceral crisis. To address these gaps and to inquire whether practicing patterns for HER2+/HR+ patients have evolved according to results of clinical trials, we capitalized on a large clinical database of a geographically dispersed network of community-based oncology practices.

Methods

Study design

This was a retrospective observational cohort study that used data from the McKesson Specialty Health's iKnowMed (iKM) electronic health record (EHR) database, which is used in most oncology network practices in the United States. The US Oncology Network is supported by McKesson Specialty Health, a division of McKesson Corporation.

The EHR data captures outpatient practice encounter history for patients who are under care, including diagnosis, therapy administration, line of therapy, patient demographics and clinical information such as stage at diagnosis, comorbidities, and performance status information. First-line treatment was defined as all treatment given to the patient prior to progression and transition to second line of therapy. For example, if a patient was initiated on chemotherapy with HER2+ targeted therapy and then switched to hormone therapy prior to progression to second line, all 3 types of agents (chemotherapy, HER2+ targeted, or hormone therapy) would be captured as first-line treatment. Within the US Oncology practices, a line of therapy (LOT) is usually associated with metastatic disease, however some patients may have had metastatic disease and not have their line of therapy recorded and hence those patients were retained in the initial sample. Patients could have received all 3 classes of drugs in the first line of therapy; that is, they may have initiated treatment with a combination of chemotherapy and targeted therapy followed by hormone therapy.

Inclusion and exclusion criteria

Inclusion criteria included women with newly diagnosed HER2+/HR+ MBC who initiated first-line treatment for MBC between January 1, 2007 and June 30, 2010, with follow-up until July 31, 2010. Other inclusion criteria were postmenopausal status before or at initiation of first-line treatment, and receiving care at a practice that used the full EHR capabilities of iKM. Premenopausal women were excluded in these analyses because aromatase inhibitors such as anastrozole and letrozole are not indicated in these patients and premenopausal women with HER2+/HR+ disease do not have a dual blockade option (HER2 agent plus HR agent) within their choices of therapy. Patients enrolled in clinical trials and/or receiving care for other primary tumors as well as with inconclusive or missing estrogen/progesterone or HER2 status were excluded.

Visceral crisis

Although "visceral crisis" is a subjective term, we segregated patients based on prespecified selection criteria that were clearly defined as liver metastasis, lymphangitic pulmonary metastasis, or brain metastasis, and subjected this study group to chart review. On this basis, we stratified patients into 2 study groups based on presence or absence

of visceral crisis. Because the EHR database does not capture the presence or absence of visceral crisis, patients were classified as with and without visceral crisis based on the following definitions using a text search of the patient's electronic charts and physician progress notes: liver metastasis; bone marrow replacement (identified by "pancytopenia" in patients with bone metastasis); lymphangitic lung metastasis (identified by "lymphangitic" in patients with lung metastasis); and carcinomatous meningitis (identified by "meningitis" in patients with brain metastasis). Pancytopenia was defined as a platelet count < 100 cells/μL, Hb < 8g/dL, and neutrophil count $< 1{,}500$ cells/μL. We used the iKM electronic medical record to query the location of metastasis, and this variable is reported as Bone, Lung, Brain, Other/Multiple, or Missing, with the latter term denoting that at time of query of the chart and progress notes, the information regarding the location of the metastasis could not be discerned. We reviewed 438 patients' charts and physician progress notes for identifying visceral crisis.

Data analysis

Descriptive analyses of the treatment cohort were generated for all key patient demographics, disease attributes and treatment patterns for patients with visceral crisis and those without visceral crisis (nonvisceral crisis). Data were also analyzed by ECOG performance status and year of initiation of therapy to investigate whether treatment patterns vary by subgroups defined on these characteristics. Data were analyzed using SAS version 9.1. This study was approved by the institutional review board of US Oncology/McKesson Specialty Health.

Results

Study population

There were a total of 14,739 patients with metastatic breast cancer (MBC) treated within the US Oncology Network. Some patients had an unknown line of therapy, that is, they did not have any line of therapy recorded. Of the total 14,739 MBC patients identified, 13,270 women who were HER2- and HR-, or HER2+ and HR-, or HER2- and HR+ were excluded from the study. Of the remaining 1,469 patients who were HER2+ and HR+, 783 initiated a first line of therapy during January 1, 2007 and June 30, 2010. Of the 783 patients, 345 patients were excluded (69 patients in clinical trials, 55 patients treated for other primary tumors, and 221 patients were premenopausal or perimenopausal prior to the initiation of a first line of therapy). The remaining sample comprised 438 patients, of whom we excluded 37 patients who did not have evidence of metastasis and their line of therapy was characterized as "unknown." In addition, 54 patients were excluded because they received trastuzumab in the adjuvant setting and were incorrectly classified in the EMR system as MBC patients.

We further identified 76 patients with liver metastasis and characterized those patients as having visceral crisis. An additional 13 patients had evidence of visceral crisis identified through extensive chart reviews and these 89 patients were characterized as HER2+/HR+ MBC patients with visceral crisis. Consequently, the final sample comprised 347 patients, of which 89 and 258 had or lacked evidence of visceral crisis, respectively.

Table 1 describes the demographic and clinical characteristics of the study population and by evidence of visceral crisis. The mean age of the patients in the overall study cohort was 62 years. About 89% of the patients were older than 50 years, 62% had good performance status (ECOG = 0) at start of first-line therapy, and 44% had metastasis to the bone. In the retrospective analyses of the charts, we were unable to discern the location of the metastasis in 31% (n = 109) of the patients, and of these 7% (n = 8) were categorized with visceral crisis (Table 1).

First-line therapies by visceral crisis status

Figure 1 (p 78) depicts the type of anticancer treatment received in HER2+/HR+ postmenopausal MBC patients stratified by presence or absence of visceral crisis. A combination of chemotherapy, targeted, and hormone therapy was the most frequently used first-line treatment strategy in both study groups (37% and 32% with and without visceral crisis, respectively). A combination of hormone and targeted therapy was the second most frequently received treatment regimen for patients without visceral crisis patients (19%), whereas chemotherapy plus targeted therapy was the second most frequently received treatment regimen for patients with visceral crisis (21%). The proportion of patients receiving only single agent regimens (hormone, chemotherapy, or targeted therapy) was low in both groups.

Table 2 (p 79) describes the mode of administration of therapy and specific drugs that were used in the study population stratified by presence versus absence of visceral crisis. More than half of the patients in both the study groups (64% nonvisceral; 62% visceral) had treatment with intravenous plus oral regimens. A higher proportion of patients without visceral crisis (15%) were treated with oral regimens only, compared with those with visceral crisis (8%). Treatment with taxanes, especially paclitaxel, dominated the chemotherapy-containing regimens in patients with (39%) or without visceral crisis (24%). Trastuzumab was the most frequently used targeted therapy in both study groups (77% and 66% of patients with and without visceral crisis, respectively). About 8% of the

TABLE 1 Patient demographic and clinical characteristics of patients with and without visceral crisis initiating a first-line therapy

Characteristic	Total N (%)	Without visceral crisis n (%)	With visceral crisis n (%)
No. of patients	347	258	89
Age,[a] y			
Mean (SD)	61.9 (10.9)	61.8 (11.1)	62.1 (10.6)
Median (range)	59.8 (33.2–87.9)	59.2 (33.2–87.9)	60.7 (38.4–81.6)
≤ 50, no. (%)	38 (11)	27 (10)	11 (12)
> 50, no. (%)	309 (89)	231 (90)	78 (88)
Height, mean (SD), in.	64.2 (2.7)	64.2 (2.8)	63.9 (2.5)
Weight, mean (SD), lb	167.7 (46.3)	168.9 (47.4)	164.2 (43)
ECOG Performance Status			
0	215 (62)	168 (65)	47 (53)
1	105 (30)	70 (28)	35 (39)
2	21 (6)	14 (5)	7 (8)
3	3 (1)	3 (1)	–
Missing	3 (1)	3 (1)	–
Stage at diagnosis			
I	49 (14)	39 (15)	10 (11)
II	82 (24)	59 (23)	23 (26)
III	61 (17)	46 (18)	15 (17)
IV	139 (40)	100 (39)	39 (44)
Unknown	16 (5)	14 (5)	2 (2)
Location of metastasis[b]			
Bone	152 (44)	104 (40)	48 (54)
Lung	26 (7)	24 (9)	2 (2)
Brain	9 (3)	8 (3)	1 (1)
Other/multiple	51 (15)	21 (8)	30 (34)
Missing	109 (31)	101 (39)	8 (9)
Tumor size			
1a	9 (3)	6 (2)	3 (3)
1b	15 (4)	14 (5)	1 (1)
1c	71 (20)	54 (21)	17 (19)
2	116 (33)	86 (33)	30 (35)
3	46 (13)	36 (14)	10 (12)
4a	5 (1)	2 (1)	3 (3)
4b	24 (8)	17 (1)	7 (8)
4c	7 (2)	5 (2)	2 (2)
4d	15 (5)	10 (4)	5 (5)
Unknown	26 (7)	17 (6)	9 (10)
Missing	13 (4)	11 (3)	2 (2)
Tumor grade			
Well differentiated	11 (3)	6 (2)	5 (4)
Moderately differentiated	125 (36)	95 (37)	30 (34)
Poorly differentiated	155 (45)	116 (45)	39 (45)
Unknown/cannot be assessed	26 (7)	20 (7)	6 (7)
Missing	30 (9)	21 (9)	9 (10)

ECOG, Eastern Cooperative Oncology Group.
[a] Age at first-line therapy. [b] As documented in iKM and not through chart reviews.

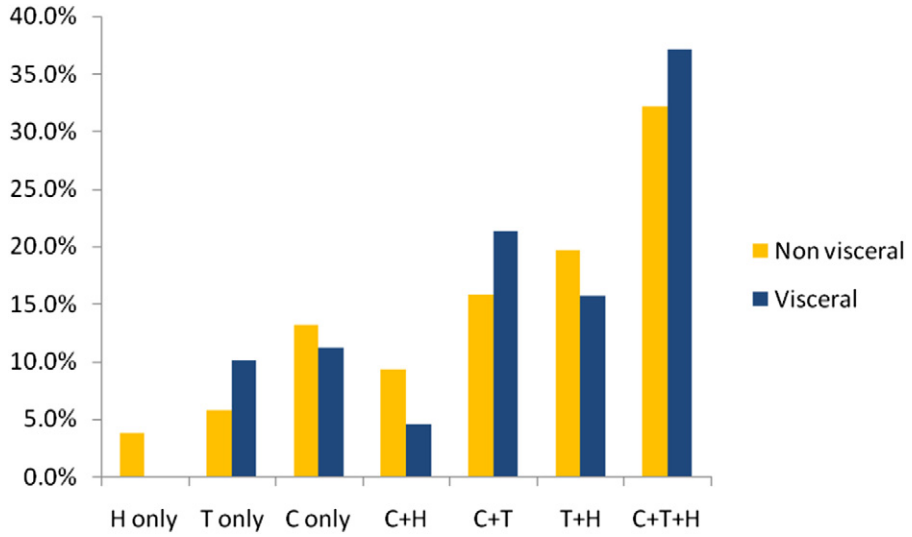

FIGURE 1 First-line therapies in HER2+/HR+ postmenopausal MBC patients with and without visceral crisis. Abbreviations: C, chemotherapy; H, hormone therapy; T, targeted therapy.

patients in both study groups received lapatinib. Aromatase inhibitors were the most frequently used hormone therapy in both cohorts (17% and 23% of patients with and without visceral crisis, respectively). Corresponding proportions for letrozole were 28% and 26%, respectively.

First-line therapies over time

We further examined whether patterns of treatment differed by performance status and by year of diagnosis in patients with or without visceral crisis (Table 3; p 80). There was no observable trend in the treatment patterns when stratified by ECOG performance status (ECOG = 1-3 vs ECOG = 0). However, when stratified by year of diagnosis, in both study groups, we observed that the use of trastuzumab decreased over time (nonvisceral: 71% in 2007 vs 55% in 2010, visceral: 77% in 2007 vs 66% in 2010) whereas the use of lapatinib increased over time (nonvisceral: 4% in 2007 vs 18% in 2010, visceral: 4% in 2007 vs 11% in 2009).

Discussion

Compared with the management of HR-negative breast cancer, the clinician is frequently faced with a decision regarding the best initial therapy for a woman with HER2+/HR+ disease. HR-bearing breast tumors with HER2 overexpression and/or amplification associates strongly with endocrine treatment failure and mortality as these tumors are more aggressive and may benefit from combined modality therapy.[20,21] Although the National Comprehensive Cancer Network (NCCN) guidelines recommend chemotherapy in combination with HER2 targeted therapy as first-line therapy, the current practice in the wider oncology community is largely unknown. To address this gap, we characterized treatment choices for HER2+/HR+ advanced breast cancer in a large community oncology setting. There are 4 key findings of this study: first, the heterogeneity of treatment choices by clinicians for HER2+/HR+ advanced breast cancer patients; second, the high prevalence of the use of concurrent chemotherapy-targeted-endocrine treatment as first-line therapy for such patients, a strategy for which no data exist and which is not endorsed by NCCN or any other guideline; third, patients with better performance status or patients with visceral crisis were more likely to receive combination treatment including chemotherapy; and fourth, treatment choices changed over time, mirroring the concurrent advances made through clinical trials.

Thus, the physicians we studied in the community oncology setting used a multimodality therapy (therapy that combines more than 1 method of treatment) as first-line therapy for HER2+/HR+ MBC patients irrespective of visceral crisis status. Overall, 18% of the patients were treated with a combination of hormone and targeted therapy and did not have the inclusion of chemotherapy in their first-line treatment setting. When targeted therapy was prescribed, trastuzumab-containing regimens dominated the anti-HER2 treatment. When chemotherapy was prescribed, paclitaxel was the most commonly used cytotoxic chemotherapy. When HR+ targeted therapy was prescribed, aromatase inhibitors such as anastrazole and/or letrozole were the most commonly used hormone therapies in this postmenopausal study population.

The clinical success of trastuzumab exemplifies the potential role of targeted therapy. Nevertheless, many questions remain, including optimal duration of therapy, dosage schedule, chemotherapy combination, and means of overcoming trastuzumab resistance. Results from the TAnDEM trial demonstrated an improved progression free survival but greater incidence of serious adverse events among patients receiving trastuzumab and anastrazole.[7] Results from the current study indicate that the rate of use of trastuzumab for the HER2+/HR+ MBC patients decreased between 2007 and 2010 in patients with and without visceral crisis. Conversely, use of lapatinib in

TABLE 2 Therapies in HER2+ or HR+ patients with metastatic breast cancer with and without visceral crisis

	Without visceral crisis n (%)	With visceral crisis n (%)
No. of patients	258	89
Mode of administration		
IV only	53 (20)	27 (30)
Orals only	39 (15)	7 (8)
IV plus orals	166 (64)	55 (62)
Targeted therapy[a]		
Trastuzumab	170 (66)	68 (77)
Lapatinib	21 (8)	7 (8)
Bevacizumab	6 (2)	1 (1)
Chemotherapy (selected drugs)[a]		
Paclitaxel	63 (24)	35 (39)
Carboplatin	40 (15)	21 (23)
Docetaxel	48 (19)	8 (9)
Capecitabine	43 (16)	5 (5)
Vinorelbine	24 (9)	10 (11)
Cyclophosphamide	18 (7)	2 (2)
Gemcitabine	1 (0.3)	3 (3)
5-FU	3 (1)	1 (1)
Hormone therapy[a]		
Aromatase inhibitors		
Anastrozole	60 (23)	15 (17)
Letrozole	67 (26)	25 (28)
Exemestane	27 (10)	8 (9)
Estrogen receptor antagonist/ antiestrogens		
Fulvestrant	33 (13)	17 (19)
Tamoxifen	23 (9)	5 (5)

5-FU, fluorouracil; HER2+, human epidermal growth factor receptor 2-positive; HR+, hormone receptor-positive; IV, intravenous.
[a] Monotherapy or in combination with other drugs.

this setting increased over this period in patients with and without visceral crisis, consistent with the timing of the presentation of results of randomized trials demonstrating the efficacy of lapatinib containing regimens (lapatinib plus capecitabine and lapatinib plus letrozole) in HER2+ metastatic breast cancer.[11,12,22]

In this study, chemotherapy in addition to hormone and targeted therapy was the most frequently used regimen (37% and 32% in patients with and without visceral crisis, respectively). Combination chemotherapy in metastatic breast cancer patients may be effective in improving response rates, time to progression and overall survival; however, aggressive upfront therapy is not always the best choice for every patient. Moreover, combination treatments may also result in increased toxicity. Those who have progressed on hormone therapy, those with HR-negative tumors, and those with visceral metastases are ideal candidates for cytotoxic agents.[23] Patients in this study were treated with an extensive variety of chemotherapeutic agents as first-line therapy irrespective of visceral crisis. Among cytotoxic agents, taxanes (paclitaxel and docetaxel) have proven efficacy and tolerability and have a valuable role in anthracycline-resistant patients.[24-29] Taxane-containing regimens dominated the chemotherapy regimens in this study and were administered to about 43% of the patients with visceral crisis and 48% of those without visceral crisis in the first-line settings. The heterogeneity in the regimens prescribed precluded large sample sizes for robust statistical analyses to link specific therapeutic combinations with outcomes.

This study has limitations. The iKM data may be limited in various aspects because the data are collected on an intent-to-treat basis. Moreover, inadequate or inaccurate codes in the database may introduce some level of misclassification bias. In addition, due to the variable duration of first-line therapy with multiple therapeutic target strategies, and inadequate follow-up time, the actual first-line treatment for some patients may not have been fully captured. For example, if a patient was on chemotherapy and HER2 targeted therapy it is possible that the patient may not have received endocrine therapy during the study period but would receive it eventually. Hence our data may not reflect their ultimate treatment plan.

Furthermore, because of the manner in which data was collected there could be some misclassification of patients with visceral crisis. For example, the term "missing" for 'location of metastasis' in Table 2 refers to the fact that we were unable to ascertain the precise site of metastasis. Although our chart reviews were exhaustive and we placed a special emphasis on identifying patients with liver metastasis, it is conceivable that a patient could have had liver metastasis that was inadvertently missed during review and/or that the physician had not recorded that point. However, it is known that most patients with metastatic breast cancer do not present with visceral crisis, and in accord with this, only about 26% of our selected population were classified as having visceral crisis. This proportion suggests that it is unlikely that we inadvertently misclassified individuals with liver metastasis or other evidence of visceral crisis to the missing or nonvisceral crisis group, and conversely, individuals without evidence visceral crisis to the nonvisceral crisis group.

TABLE 3 Subanalysis of treatment patterns for HER2+ and HR+ patients with metastatic breast cancer with or without visceral crisis stratified by ECOG status and year of diagnosis

		Targeted therapy, n (%)		Chemotherapy, n (%)				Drug class, n (%)			
	n	Trastuzumab	Lapatinib	Paclitaxel	Capecitabine	Any CT	Any HT	CT+TT	HT+TT	CT+TT+HT	CT+HT
Without visceral crisis											
ECOG status[a]											
0	168	124 (74)	10 (6)	50 (30)	19 (11)	118 (70)	113 (67)	29 (17)	36 (21)	60 (36)	11 (6)
1-3	87	46 (53)	11 (12)	13 (15)	24 (28)	62 (71)	51 (58)	12 (14)	15 (17)	23 (26)	11 (12)
Year											
2007	49	35 (71)	2 (4)	11(22)	6 (12)	30 (61)	32 (65)	5 (10)	14 (28)	14 (29)	3 (6)
2008	82	60 (74)	7 (9)	22 (27)	12 (15)	63 (76)	48 (58)	16 (19)	12 (14)	31 (38)	4 (5)
2009	83	51 (61)	4 (5)	20 (24)	16 (19)	61 (73)	59 (71)	14 (17)	6 (13)	25 (30)	13 (15)
2010	44	24 (55)	8 (18)	10 (23)	9 (21)	28 (63)	28 (63)	6 (13)	(20)	13 (30)	3 (6)
With visceral crisis											
ECOG status											
0	47	37 (78)	4 (8)	12 (25)	3 (6)	29 (61)	26 (55)	8 (17)	10 (21)	13 (27)	3 (6)
1-3	42	31 (73)	3 (7)	23 (54)	2 (4)	36 (85)	25 (59)	11 (26)	4 (9)	19 (45)	2 (4)
Year											
2007	22	17 (77)	1 (4)	10 (45)	3 (13)	16 (72)	11 (50)	5 (22)	2 (9)	9 (40)	0 (0)
2008	30	21 (70)	3 (10)	9 (30)	2 (6)	19 (63)	15 (50)	6 (20)	4 (13)	8 (26)	3 (10)
2009	28	25 (89)	3 (11)	12 (42)	–	18 (64)	20 (71)	6 (21)	7 (25)	12 (42)	1 (3)
2010	9	6 (66)	–	4 (44)	–	7 (77)	5 (55)	2 (22)	1 (11)	3 (33)	1 (11)

CT, chemotherapy; ECOG, Eastern Cooperative Oncology Group; HT, hormone therapy; TT, targeted therapy.
[a] 3 patients with missing ECOG status information.

Another potential limitation is with respect to the limited capture of oral medications and infusional treatment in the iKM database. These potential limitations are offset by the large sample size studied, and possible generalizability of our results as the US Oncology Network is a large geographically dispersed network of community-based oncology practices, treating more than 750,000 patients annually, and accounting for nearly 15% of all cancer patients in the U.S.

Conclusion

We describe treatment patterns in postmenopausal HER2+/HR+ MBC in the community oncology setting. Although most patients in the community will receive chemotherapy in combination with therapies that target HER2+/HR+ disease, there is a large percentage of patients who are treated in the community and who do not receive chemotherapy as first-line therapy. The heterogeneity in the prescribed regimens suggests a lack of a universal standard of care for patients with advanced HER2+/HR+ MBC. Additional clinical studies of regimens used commonly are needed to refine our understanding of effective therapies, the use of which results in tumor regression, prolongation of life, and minimal toxicity. The strengths of this study include the use of clinically detailed EMR data that accounted for a very extensive characterization of the treatment clinical and demographic characteristics of the patient population. As opposed to claims-based data sources, the use of oncology-specific EMR data, as is available through iKM, provides data that are similar to those collected in randomized controlled trials. As community-based clinical practice may differ from the clinical trial setting, our results provide insights into how clinical trial treatment protocols are translated in the real-world setting.

Acknowledgments

The authors thank William Lopez, MS, Yasir Nagarwala, MD, Michael Forsyth, RPh, and Menaka Bhor, PhD, for analyzing the data, study design, data extraction, and providing editorial support. This study was accepted as an e-publication: Sharma PP, Sail K, Delea TE, Forsyth MT, Halm M, Nagarwala YM, Lopez W, Patt DA. Patterns of care and patient characteristics in post-menopausal women with HER2+ and hormone receptor-positive (HR+) metastatic breast cancer (MBC). ASCO Abstract: ASCO Annual Meeting June 3-7, 2011 Chicago.

References

1. Howlader N, Noone AM, Krapcho M, et al, eds. SEER Cancer Statistics Review: 1975-2008, National Cancer Institute. Be-

thesda, MD. http://seer.cancer.gov/csr/1975_2008/. Based on November 2010 SEER data submission. Accessed January 12, 2012.
2. American Cancer Society. Cancer Facts and Figures 2010. Atlanta, GA: American Cancer Society, 2010.
3. Benz CC, Scott GK, Sarup JC, et al. Estrogen-dependent, tamoxifenresistant tumorigenic growth of MCF-7 cells transfected with HER2/neu. *Breast Cancer Res Treat*. 1992;24:85-95.
4. Pietras RJ, Arboleda J, Reese DM, et al. HER-2 tyrosine kinase pathway targets estrogen receptor and promotes hormone independent growth in human breast cancer cells. *Oncogene*. 1995;10: 2435-2446.
5. Yarden Y, Sliwkowski MX. Untangling the ErbB signalling network. *Nat Rev Mol Cell Biol*. 2001;2:127-137.
6. Hynes NE, Lane HA. ErbB receptors and cancer: the complexity of targeted inhibitors. *Nat Rev Cancer*. 2005;5:341-54.
7. Kaufman B, Mackey JR, Clemens MR, et al. Trastuzumab plus anastrozole versus anastrozole alone for the treatment of postmenopausal women with human epidermal growth factor receptor 2-positive, hormone receptor-positive metastatic breast cancer: Results from the randomized phase III TAnDEM study. *J Clin Oncol*. 2009;27:5529-5537.
8. Gligorov J, Lotz JP. Optimal treatment strategies in postmenopausal women with hormone-receptor-positive and HER2-negative metastatic breast cancer. *Breast Cancer Res Treat*. 2008; 112(suppl 1):53-66.
9. Curran MP. Lapatinib in postmenopausal women with hormone receptor-positive, HER2-positive metastatic breast cancer. *Drugs*. 2010;70:1411-1422.
10. Sherrill B, Amonkar MM, Sherif B, et al. Quality of life in hormone receptor positive HER2+ metastatic breast cancer patients after treatment with letrozole alone or in combination with lapatinib. *Oncologist*. 2010;15:944-953.
11. Schwartzberg LS, Franco SX, Florance A, et al. Lapatinib plus letrozole as first-line therapy for HER-2+ hormone receptor-positive metastatic breast cancer. *Oncologist*. 2010;15:122-129.
12. Johnston S, Pippen J Jr, Pivot X, et al. Lapatinib combined with letrozole versus letrozole and placebo as first-line therapy for postmenopausal hormone receptor-positive metastatic breast cancer. *J Clin Oncol*. 2009;27:5538-5546.
13. Slamon DJ, Leyland-Jones B, Shak S, et al. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. *N Engl J Med*. 2001;344:783-792.
14. Di Leo A, Gomez HL, Aziz Z, et al. Phase III, double-blind, randomized study comparing lapatinib plus paclitaxel with placebo plus paclitaxel as first-line treatment for metastatic breast cancer. *J Clin Oncol*. 2008;26:5544-5552.
15. Slamon DJ, Godolphin W, Jones LA, et al. Studies of the HER-2/neu proto-oncogene in human breast and ovarian cancer. *Science*. 1989;244:707-712.
16. Marty M, Cognetti F, Maraninchi D, et al. Randomized phase II trial of the efficacy and safety of trastuzumab combined with docetaxel in patients with human epidermal growth factor receptor 2-positive metastatic breast cancer administered as first-line treatment: the M77001 study group. *J Clin Oncol*. 2005;23:4265-4274.
17. Andersson M, Lidbrink E, Bjerre K, et al. Phase III randomized study comparing docetaxel plus trastuzumab with vinorelbine plus trastuzumab as first-line therapy of metastatic or locally advanced human epidermal growth factor receptor 2–positive breast cancer: The HERNATA Study. *J Clin Oncol*. 2011;29: 264-271.
18. Guan ZZ, Xu B, Arpornwirat W, et al. Overall survival benefit observed with lapatinib (L) plus paclitaxel (P) as first-line therapy in patients with HER2-overexpressing metastatic breast Cancer. Presented at the San Antonio Breast Cancer Symposium, San Antonio, TX, 2010.
19. Blackwell KL, Burstein HJ, Storniolo AM, et al. Randomized study of lapatinib alone or in combination with trastuzumab in women With ErbB2-Positive, trastuzumab-refractory metastatic breast cancer. *J Clin Oncol*. 2010;28:1124-1130.
20. Slamon DJ, Godolphin W, Jones LA, et al. Studies of the HER-2/neu proto-oncogene in human breast and ovarian cancer. *Science*. 1989;244:707-712.
21. Yu D, Hung MC. Overexpression of ErbB2 in cancer and ErbB2-targeting strategies. *Oncogene*. 2000;19:6115-6121.
22. Geyer CE, Forster J, Lindquist D, et al. Lapatinib plus capecitabine for HER2-positive advanced breast cancer. *New Engl J Med*. 2000;355:2733-2743.
23. Wilcken N, Dear R. A summary of all randomized trials reported 2000-2007. *Eur J Cancer*. 2008;44:2218-2225.
24. Nabholtz JM, Senn HJ, Bezwoda WR. Prospective randomized trial of docetaxel versus mitomycin plus vinblastine in patients with MBC progressing despite previous anthracycline containing chemotherapy. *J Clin Oncol*. 1999;17:1413-1424.
25. Sjostrom J, Blomqvist C, Mouridsen H, et al. Docetaxel compared with sequential methotrexate and 5-flurouracil in patients with advanced breast cancer after anthracycline failure: a randomized phase III study with crossover on progression by the Scandinavian Breast Group. *Eur J Cancer*. 1999;35:1194-1201.
26. Chan S, Friedrichs K, Noel D, et al. Prospectove randomized trial of docetaxel versus doxorubicin in patients with metastatic breast cancer. *J Clin Oncol*. 1999;17:2341-2354.
27. Dieras V, Marty M, Tubiana N, et al. Phase II randomized study paclitaxel versus mitomycin in advanced breast cancer. *Semin Oncol*. 1995;22(4)(suppl 8):33-39.
28. Seidman AD, Reichman BS, Crown JP, et al. Paclitaxel as second and subsequent therapy for metastatic breast cancer: activity independent of prior anthracycline response. *J Clin Oncol*. 1995;13: 1152-1159.
29. Clemons M, Leahy M, Valle J, et al. Review of recent trials chemotherapy for advanced breast cancer: the Taxanes. *Eur J Cancer*. 1997;33:2171-2182.