

Background

About 15-20% of subjects with breast cancer have human epidermal growth factor receptor 2 (HER-2) positive tumors, which are considered more aggressive and less responsive to standard adjuvant therapy.

The treatment guidelines recommend routine testing of HER-2 on newly diagnosed and metastatic breast cancer.

Currently, both immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) are performed to identify HER-2 positive breast cancer, which is responsive to trastuzumab (Herceptin) therapy.

Medicare covers the use of trastuzumab for the treatment of metastatic breast cancer only when the HER-2 status has been confirmed through IHC or FISH testing.

Objective

Explore the utility of Medicare claims data in analyzing the role of HER-2 testing, treatment and outcomes in subjects with metastatic breast cancer.

Evaluate adherence to the Medicare coverage policies.

Approach

A retrospective claims database study.

Data Source

The Medicare Standard Analytic File (SAF) from the Centers for Medicare and Medicaid Services (CMS) is a randomly-selected 5% sample of all Medicare beneficiaries.

Medicare beneficiaries consisted of individuals ≥ 65 years, those eligible for disability, and/or those with end stage renal disease.

All claims in the 2005 SAF were used to identify hospital outpatient, physician, and laboratory claims for the presence of IHC, FISH procedures, or trastuzumab use.

Identification of Study Cohorts

The International Classification of Disease, Ninth Revision (ICD-9) codes 174-175 were used to define subjects with primary diagnoses of malignant breast cancer (MBC) in the first two quarters of 2005.

Subjects with diagnoses of MBC in 2004 were excluded.

The Current Procedural Terminology (CPT) codes 88342, 88360, 88361 and 88365 were used to identify IHC test and FISH test while the Healthcare Common Procedure Coding System (HCPCS) code J9355 was used to ascertain trastuzumab use in the entire year of 2005.

Statistical Analysis

Descriptive statistics were carried out for demographics, mortality, and Medicare payments for the identified subjects.

These characteristics were compared between the following cohorts: (1) subjects receiving trastuzumab who underwent HER-2 testing and did not receive trastuzumab, (2) subjects who received trastuzumab but did not undergo HER-2 testing, and (3) subjects who underwent HER-2 testing and received trastuzumab.

Hypothesis tests for continuous variables were conducted using t tests. Chi-square tests were used to analyze categorical variables. Level of significance (alpha) for all statistical tests was set at 0.05.

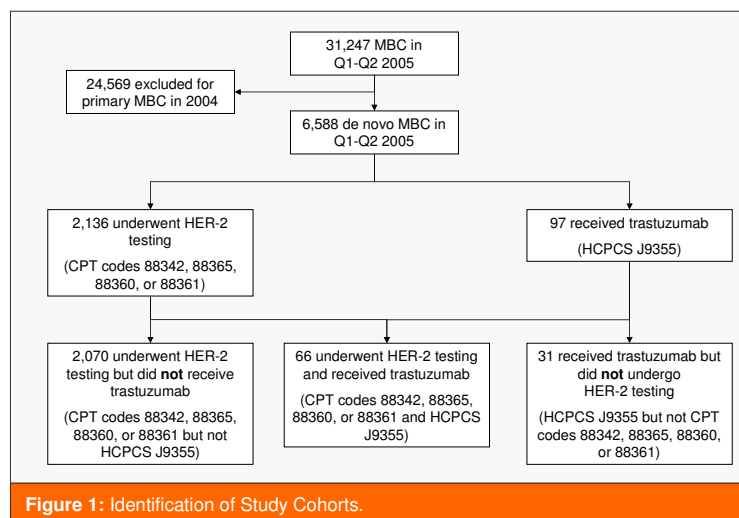


Figure 1: Identification of Study Cohorts.

Results

In the first two quarters of 2005, 31,247 subjects were diagnosed with MBC. After excluding 24,569 subjects with previous diagnoses, we obtained a total cohort of 6,588 subjects with de novo MBC (Figure 1).

Of these subjects, 2,136 underwent a HER-2 test, 97 received trastuzumab, and 66 received both in 2005.

Among the tested subjects, 1,993 (93%) received IHC alone, 6 (0.3%) received FISH alone, and 137 (6%) received both.

Compared to subjects who did not receive trastuzumab following an HER-2 evaluation, subjects receiving trastuzumab were significantly younger (41% vs. 69% ≥ 70 years, $p < 0.001$); and less likely to be African-American (5% vs. 10%, $p = 0.02$). There was no significant difference in mortality rate (2% vs. 7%, $p = 0.09$); however, the average Medicare payments in the trastuzumab cohort more than doubled those in the non-trastuzumab cohort (\$46,289 vs. \$22,560, $p < 0.001$) in 2005 (Table 1).

Among subjects receiving trastuzumab, HER-2 evaluations were identified in 66 subjects (68%). In comparison to these subjects, the non-HER-2 test cohort was comprised of significantly more subjects aged < 60 (39% vs. 12%, $p = 0.02$), and more African-American (23% vs. 5%, $p = 0.02$). It also had a higher mortality rate (10% vs. 2%, $p = 0.06$), although the difference did not reach statistical significance (Table 2).

Discussion

Our study demonstrated a variation in the clinical practice of HER-2 testing and trastuzumab treatment. We also observed a gap between the treatment guidelines and a deviation from Medicare reimbursement policy in the real-world practice.

Our study is likely to overestimate the rate of HER-2 test when each IHC or FISH claim was counted as a new test, although it might have been a re-test to confirm the previous test results.

Although trastuzumab might be administered in an inpatient setting, no HCPCS codes for injectable drugs could be identified from the inpatient claims data; therefore, these cases were not included in our analysis.

Table 1: Demographics, Mortality, and Medicare Payments among Subjects who underwent HER-2 tests.

	HER-2 Test Only (N=2,070)	Test + Trastuzumab (N=66)	P Value
Age (Year) – N (%)			<0.001
<60	87 (4.2)	8 (12.1)	
60-69	560 (27.1)	31 (47.0)	
70-79	859 (41.5)	22 (33.3)	
>80	564 (27.3)	5 (7.6)	
Race – N (%)			0.02
White	1,819 (87.9)	58 (87.9)	
African-American	197 (9.5)	3 (4.6)	
Other	52 (2.6)	5 (7.6)	
Mortality	139 (6.7)	1 (1.5)	0.09
Medicare Payment			<0.001
Mean	\$22,560	\$46,289	
Median	\$16,087	\$44,239	

Table 2: Demographics, Mortality, and Medicare Payments among Subjects who received Trastuzumab.

	Trastuzumab Only (N=31)	Test + Trastuzumab (N=66)	P Value
Age (Year) – N (%)			0.02
<60	12 (38.7)	8 (12.1)	
60-69	13 (41.9)	31 (47.0)	
70-79	5 (18.5)	22 (33.3)	
>80	1 (3.2)	5 (7.6)	
Race – N (%)			0.02
White	23 (74.2)	58 (87.9)	
African-American	7 (22.6)	3 (4.6)	
Other	1 (3.2)	5 (7.6)	
Mortality	3 (9.7)	1 (1.5)	0.06
Medicare Payment			0.09
Mean	\$37,961	\$46,289	
Median	\$33,244	\$44,239	

Conclusion

Based on a 5% sample of Medicare beneficiaries and claims data, not all patients treated with trastuzumab had a corresponding IHC or FISH test performed. Therefore, claims data alone may have limited utility in determining the role of HER-2 testing, treatment, and outcomes in patients with metastatic breast cancer.

Medicare contractors may also need to seek alternative methods to evaluate adherence to their coverage policies.

References

- Wolff AC, Hammond ME, Schwartz JN, et al. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer. *J Clin Oncol.* 2007 Jan 1;25(1):118-45.
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