Real-World Molecular Testing Rates and Patterns in Patients With Primary Advanced or Recurrent Endometrial Cancer in the United States

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ABSTRACT

PURPOSE This retrospective cohort study estimated the real-world utilization of biomarker testing among patients with primary advanced/recurrent endometrial cancer (pA/rEC) and characterized testing according to demographic and clinical characteristics.

MATERIALS AND METHODS A nationwide electronic health record–derived deidentified database was used. Records from January 1, 2013, to August 31, 2023, for women age 18 years and older with pA/rEC were searched for DNA mismatch repair (MMR)/microsatellite instability (MSI), human epidermal growth factor receptor 2 (HER2), and estrogen receptor (ER) or progesterone receptor (PR) testing; a subsample data set (advEndo Spotlight) was searched from April 1, 2013, to November 30, 2022, for additional biomolecular testing. Testing rates were reported by index year and molecular marker. Multivariate logistic regression analyses were conducted to identify characteristics associated with testing.

RESULTS The full data set included 2,982 patients, of whom 53% were age 65 years and older; most were non-Hispanic White (56%) and received care in a community setting (73%). The advEndo Spotlight subsample (n = 509) had similar characteristics. From 2013 to 2021, testing for any biomarker increased from 53% to 89% (MMR/MSI, 17% to 81%; ER/PR, 45% to 62%; HER2, 15% to 43%). Patients who received care at an academic versus community facility, had commercial/other insurance versus Medicare/Medicaid, had primary advanced versus recurrent EC, had endometrioid versus nonendometrioid carcinoma, or had no previous surgery as part of primary treatment were more likely to receive testing.

CONCLUSION Molecular testing rates in pA/rEC have increased over time, likely due in part to incorporation of biomarker testing into treatment guidelines. This highlights an unmet need to ensure universal access to testing in patients with pA/rEC. Understanding these factors can inform approaches to increase access to molecular testing and increase testing rates.

ACCOMPANYING CONTENT

Data Sharing Statement

Data Supplement

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INTRODUCTION

Endometrial cancer (EC) is the most common type of gynecologic cancer worldwide.[1] Its incidence has risen annually, with an estimated 67,880 new cases in the United States in 2024, representing 3.4% of all new cancer cases.[2] The mortality of EC also continues to rise, with the number of estimated deaths now surpassing those due to ovarian cancer.[2] Approximately 20% to 30% of patients have advanced EC upon diagnosis.[3,4] Various biomarkers can be used to inform prognosis or guide treatment in EC, including DNA mismatch repair (MMR) or microsatellite instability (MSI) status, human epidermal growth factor receptor 2 (HER2), DNA polymerase-ε catalytic subunit (POLE), AT-rich interactive domain-containing protein 1A (ARID1A), tumor protein 53 (p53/TP53), tumor mutation burden (TMB), catenin beta 1 (CTNNB1), and estrogen receptor (ER) or progesterone receptor (PR).[5,6] Approximately 25% to 30% of patients have tumors that are MMR-deficient or MSI-high (dMMR/MSI-H)[7-9]; MMR deficiency is associated with an intermediate prognosis.[5] Despite the prognostic and predictive information provided by biomarker testing,[10] limited data exist on testing rates and the relationship between patient characteristics and testing in primary advanced or recurrent EC (pA/rEC) in the United States.

This retrospective cohort study used an electronic health record (EHR)–derived database to evaluate the use and

CONTEXT

Key Objective

In real-world practice in the United States, what proportion of patients with primary advanced or recurrent endometrial cancer (EC) receive testing for key biomarkers, including DNA mismatch repair/microsatellite instability, human epidermal growth factor receptor 2, estrogen receptor or progesterone receptor, and others?

Knowledge Generated

Two samples (N = 2,982 and n = 509) were analyzed with similar results. Biomarker testing rates increased between 2013 and 2021, and certain factors (receiving care at an academic *v* community facility, commercial/other insurance *v* Medicare/Medicaid, primary advanced *v* recurrent EC, endometrioid *v* nonendometrioid carcinoma, or no previous surgery as part of primary treatment) were associated with an increased likelihood of receiving testing.

Relevance

These results highlight an unmet need of ensuring access to biomarker testing for patients with primary advanced or recurrent EC. Developing a better understanding of the factors affecting testing access can inform approaches to increase testing rates.

impact of molecular testing in EC. The primary objective was to estimate the proportion of patients with pA/rEC receiving biomarker testing in practice. Secondary objectives included the identification of demographic and clinical characteristics associated with receiving molecular testing, evaluation of the time from diagnosis to testing (among those who received molecular testing), and evaluation of the time from diagnosis to initiation of treatment for those with versus without testing (among those who received treatment). As an exploratory objective, a subgroup analysis was performed to examine the biomarker testing rate, time from diagnosis to testing, and time from diagnosis to initiation of treatment among individuals with pA/rEC.

MATERIALS AND METHODS

Data Source and Inclusion Criteria

The nationwide Flatiron Health database is an EHR-derived, deidentified, longitudinal database comprising deidentified patient-level structured and unstructured data, curated via technology-enabled abstraction. During the study period, the deidentified data originated from approximately 280 cancer clinics (approximately 800 sites of care that are predominantly community health care centers *v* academic centers) in the United States.[11-13] The database contains real-world information about patient characteristics, genomic testing and results, and health outcomes. The data are deidentified and subject to obligations to prevent reidentification and protect patient confidentiality.

Two separate data sets from the Flatiron Health database were used. The full EHR data set included data on HER2, MMR/MSI, and ER/PR testing prevalence in adult patients with pA/rEC who were diagnosed from January 1, 2013, up to 12 months before August 31, 2023 (Data Supplement, Fig S1). The advEndo Spotlight subsample data set included additional data on p53/TP53, TMB, CTNNB1, ARID1A, CDK4/6, and POLE testing for patients diagnosed with pA/rEC from April 1, 2013, up to 12 months before November 30, 2022 (Data Supplement, Fig S1) and was used to supplement the EHR data set.

No information on date of testing for the additional biomarkers in the advEndo Spotlight data set was available; the test collection date was assumed to occur any time on or after the initial EC diagnosis. Biomarker testing conducted within 6 months of advanced diagnosis was included in the analysis. Patients were included if they had a documented diagnosis of advanced EC and were age 18 years and older at the first advanced EC diagnosis (index date). Patients with concurrent primary malignancies at EC diagnosis, with unspecified or unknown stage, or who received biomarker testing ≤3 months before index date were excluded. Patients were followed up from the index date until 12 months after diagnosis, the end of the study period, or death, whichever occurred first.

Analyses

Baseline Demographic and Clinical Characteristics

Baseline characteristics were summarized descriptively. Continuous variables were described by means with standard deviations and medians with IQR. Categorical variables were defined by patient counts with percentages. Primary advanced EC was defined as newly diagnosed stage III/IV EC at initial diagnosis. Recurrent EC was defined as an initial stage I/II diagnosis that subsequently recurred (local, regional, or distant).

Statistical Analysis Approach

Differences in patient characteristics between tested and untested patients were summarized. Differences in biomarker

testing rates between tested and untested patients were characterized with standardized differences between patient clinical and demographic characteristics. Multivariate logistic regression was used to identify characteristics associated with receiving biomarker testing.

RESULTS

Baseline Demographic and Clinical Characteristics

Of 5,295 patients identified in the Flatiron Health database, 2,982 were eligible to be included in the full EHR data set (Data Supplement, Table S1). Of 917 patients in the advEndo Spotlight database, 509 were eligible to be included in the advEndo data set (Data Supplement, Table S2). Demographic characteristics were similarly distributed across the two data sets. For both data sets, the mean age was 64.7 years; most patients (full EHR and advEndo Spotlight, respectively) were non-Hispanic White (56% and 52%), had commercial insurance (79% and 75%), and received care in a community setting (73% and 76%; Table 1; Data Supplement, Table S3).

In the EHR data set, several characteristics differed significantly ($P < .05$) between tested (which included testing for HER2, MMR/MSI, and ER/PR) and untested groups, including practice type, insurance status, socioeconomic status index quintile, primary advanced versus recurrent EC diagnosis, lymphovascular invasion, cancer stage at diagnosis, Eastern Cooperative Oncology Group performance status (ECOG PS), previous surgery or radiation therapy as part of primary treatment, and year of advanced EC diagnosis (Table 1); other characteristics were similar between patients with and without testing ($P > .05$).

Biomarker Testing Rates and Types

In the full EHR data set, from 2013 to 2021, testing for any biomarker, including HER2, MMR/MSI, and ER/PR, increased from 53% to 89%. Rates for individual biomarker testing also increased during this period (Fig 1; Data Supplement, Fig S2). MMR/MSI was the most frequently tested biomarker within 6 months of diagnosis (54%), followed by ER/PR (49%) and HER2 (21%).

In the advEndo Spotlight data set, from 2013 to 2021, testing rates for other biomarkers were as follows: p53/TP53, 51%; TMB, 18%; CTNNB1, 17%; ARID1A, 18%; CDK4/6, 22%; and POLE, 22%.

In the full EHR data set, among those with test results obtained before initiation of first-line systemic therapy, the majority tested negative for HER2 (73%) and positive for ER/PR (77%); 25% were MSI-H or dMMR (Table 2). The most common test type for any assessed biomarker was immunohistochemistry (IHC; 88%), followed by next-generation sequencing (NGS; 4%; Data Supplement, Fig S3).

Factors Associated With Receipt of Biomarker Testing

In the full EHR data set, patients were significantly more likely to receive biomarker testing if they received care at an academic versus community facility (odds ratio [OR], 0.59 [95% CI, 0.47 to 0.73]), were covered by commercial or other insurance versus Medicare/Medicaid (OR, 1.51 [95% CI, 1.18 to 1.93] and 1.81 [95% CI, 1.13 to 2.90], respectively), had primary advanced versus recurrent EC (OR, 1.45 [95% CI, 1.03 to 2.06]), had endometrioid versus nonendometrioid carcinoma (OR, 1.39 [95% CI, 1.01 to 1.93]), or had no previous surgery as part of primary treatment (OR, 2.29 [95% CI, 1.83 to 2.86]), after adjusting for covariates (Fig 2). Results were similar for the advEndo Spotlight data set (Data Supplement, Fig S4).

Time to Biomarker Testing

For patients who received biomarker testing, the median times from diagnosis to test collection for HER2, MMR/MSI, and ER/PR were 16.5, 16.0, and 0 days, respectively (Table 3). Among those who had evidence for first-line systemic therapy, the median time from test result date to initiation of first-line systemic therapy ranged from 40.0 to 50.0 days. Across all three biomarkers, the median time from test result to treatment initiation was shorter for patients who initiated chemotherapy treatment than for those who initiated other treatment types (HER2, 34.0 *v* 55.0-203.0 days; MMR/MSI, 42.0 *v* 103.0-257.0 days; ER/PR, 44.0 *v* 77.5-257.0 days; Table 3).

Time to Treatment Initiation

For all patients, the median time from diagnosis to treatment initiation was longer for patients who did not receive biomarker testing compared with patients who did receive testing, except in the case of MMR/MSI (HER2, 60.0 *v* 56.0 days; MMR/MSI, 53.0 *v* 64.0 days; ER/PR, 63.0 *v* 57.0 days; Table 3).

In the advEndo Spotlight data set, among those who had evidence of first-line systemic therapy, the median times from diagnosis to treatment initiation were longer for untested patients compared with those who received testing for p53/TP53 (60.0 *v* 52.0 days), TMB (58.0 *v* 50.5 days), CTNNB1 (59.0 *v* 49.0 days), ARID1A (58.0 *v* 50.5 days), CDK4/6 (57.0 *v* 52.0 days), and POLE (59.0 *v* 47.0 days; Data Supplement, Fig S5).

Biomarker Testing Rate and Results by Recurrent Versus Primary Advanced EC

In the full EHR data set, the biomarker testing rate was higher among patients with primary advanced versus recurrent EC for MMR/MSI and HER2 (Data Supplement, Table S4). However, testing type was similar among those with primary advanced versus recurrent EC for MMR/MSI and ER/PR. For HER2, almost half of the patients (49%) with

TABLE 1. Demographic and Clinical Characteristics of the Full EHR Data Set Overall and by Biomarker Testing Status (tested *v* untested)

Baseline Characteristic	Overall (N = 2,982)	Any Assessed Biomarker[a] (n = 2,165)	No Biomarker Test (n = 817)	*P*[b]
All patients, No. (%)	2,982 (100)	2,165 (73)	817 (27)	
Age, years, mean (SD)	64.7 (10.2)	64.6 (10.2)	65.2 (11.2)	.125
Age groups, years, No. (%)				.301
18-45	137 (5)	102 (5)	35 (4)	
46-64	1,271 (43)	939 (43)	332 (41)	
≥65	1,574 (53)	1,124 (52)	450 (55)	
Region of the United States, No. (%)				.192
Northeast	268 (9)	185 (9)	83 (10)	
Midwest	357 (12)	245 (11)	112 (14)	
South	1,067 (36)	781 (36)	286 (35)	
West	314 (11)	235 (11)	79 (10)	
Unknown	976 (33)	719 (33)	257 (31)	
Practice type, No. (%)				<.001
Academic	793 (27)	614 (28)	179 (22)	
Community	2,189 (73)	1,551 (72)	638 (78)	
Race and ethnicity, No. (%)				.356
Asian	61 (2)	48 (2)	13 (2)	
Black or African American	416 (14)	303 (14)	113 (14)	
Hispanic or Latino	187 (6)	125 (6)	62 (8)	
Non-Hispanic White	1,661 (56)	1,209 (56)	452 (55)	
Other race	149 (5)	114 (5)	35 (4)	
Unknown	508 (17)	366 (17)	142 (17)	
Insurance status, No. (%)[c]				.025
Commercial	2,353 (79)	1,730 (80)	623 (76)	
Medicare/Medicaid	378 (13)	252 (12)	126 (15)	
Other payer	144 (5)	111 (5)	33 (4)	
Unknown	107 (4)	72 (3)	35 (4)	
Socioeconomic status index quintile, mean (SD)	3.0 (1.4)	3.0 (1.4)	2.9 (1.5)	.003
Year of first advanced diagnosis, No. (%)				<.001
2013	228 (8)	118 (5)	110 (13)	
2014	316 (11)	160 (7)	156 (19)	
2015	348 (12)	211 (10)	137 (17)	
2016	375 (13)	244 (11)	131 (16)	
2017	370 (12)	281 (13)	89 (11)	
2018	339 (11)	272 (13)	67 (8)	
2019	355 (12)	300 (14)	55 (7)	
2020	353 (12)	318 (15)	35 (4)	
2021	298 (10)	261 (12)	37 (5)	
ECOG PS, No. (%)				<.001
0	1,283 (43)	965 (45)	318 (39)	
1	769 (26)	575 (27)	194 (24)	
2+	263 (9)	203 (9)	60 (7)	
Missing	667 (22)	422 (19)	245 (30)	
Recurrent *v* primary advanced EC, No. (%)				<.001
Recurrent	330 (11)	185 (9)	145 (18)	
Primary advanced	2,652 (89)	1,980 (91)	672 (82)	
Tumor stage at diagnosis				<.001
I	296 (10)	166 (8)	130 (16)	
II	34 (1)	19 (1)	15 (2)	

(continued on following page)

TABLE 1. Demographic and Clinical Characteristics of the Full EHR Data Set Overall and by Biomarker Testing Status (tested *v* untested) (continued)

Baseline Characteristic	Overall (N = 2,982)	Any Assessed Biomarker[a] (n = 2,165)	No Biomarker Test (n = 817)	*P*[b]
III	1,819 (61)	1,334 (62)	485 (59)	
IV	833 (28)	646 (30)	187 (23)	
Tumor grade, No. (%)				.647
Well differentiated	516 (17)	376 (17)	140 (17)	
Moderately differentiated	791 (27)	567 (26)	224 (27)	
Poorly differentiated or undifferentiated	646 (22)	481 (22)	165 (20)	
Unknown	1,029 (35)	741 (34)	288 (35)	
Histology, No. (%)				.159
Endometrioid carcinoma	1,804 (60)	1,327 (61)	477 (58)	
Nonendometrioid carcinoma	1,178 (40)	838 (39)	340 (42)	
Lymphovascular invasion, No. (%)				.032
Yes	1,161 (39)	873 (40)	288 (35)	
No	682 (23)	490 (23)	192 (24)	
Unknown	1,139 (38)	802 (37)	337 (41)	
Myometrial invasion, No. (%)				.507
Yes	1,862 (62)	1,360 (63)	502 (61)	
No	113 (4)	77 (4)	36 (4)	
Unknown	1,007 (34)	728 (34)	279 (34)	
Previous surgery for the primary treatment, No. (%)	828 (28)	495 (23)	333 (41)	<.001
Previous radiotherapy as part of primary treatment, No. (%)	151 (5)	94 (4)	57 (7)	.005

Abbreviations: EC, endometrial cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; EHR, electronic health record; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; MMR, DNA mismatch repair; MSI, microsatellite instability; PR, progesterone receptor; SD, standard deviation.

[a]Assessed biomarkers included HER2, MMR/MSI, and ER/PR.

[b]*P* value compared those who received any biomarker assessment (HER2, MMR/MSI, or ER/PR) versus those with no biomarker tests.

[c]Note that Medicare Advantage, Medicare Supplement, Medicare Part D, Managed Medicaid, and Managed Government plans are generally offered by commercial payers and are captured in the Commercial insurance category. The Other insurance category included self-pay, workers' compensation, other government program, and patient assistance program.

recurrent EC were tested by NGS, while almost half of the patients (48%) with primary advanced EC were tested by IHC (Data Supplement, Table S4). Test results for HER2, MMR/MSI, and ER/PR were similar among patients with primary advanced versus recurrent EC (Data Supplement, Table S5).

DISCUSSION

Previous studies assessed molecular testing patterns of patients with EC in other parts of the world, including Europe.[14,15] To our knowledge, this is the first large real-world study to analyze biomarker testing for patients with EC in the United States. Molecular testing rates have increased over time, indicating a continuous trend toward personalized treatment decisions. The testing rate for any of HER2, MMR/MSI, or ER/PR in the full EHR data set increased from 53% in 2013 to 89% in 2021, with MMR/MSI being the most frequently assessed biomarker during the time frame of this analysis.

The development of the Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE) classification scheme may have driven the increase in testing over time. ProMisE, a sequential classification process introduced in 2017, assigns patients with EC into prognostic groups on the basis of certain mutations and protein expression (dMMR, *POLE* exonuclease domain–mutated, *p53/TP53* wild-type, or *p53/TP53*-mutated).[16] During the time frame of this analysis, EC treatment guidelines have shifted to include molecular testing as part of the initial evaluation,[17,18] possibly contributing to an increase in molecular testing rates.

Increased biomarker testing in EC may have also been driven by an increased focus on evaluating targeted therapies in clinical trials during the time frame of this analysis. In 2018, a phase II study (ClinicalTrials.gov identifier: NCT01367002) showed that trastuzumab plus carboplatin-paclitaxel increased progression-free survival (PFS) versus carboplatin-paclitaxel alone (median PFS, 12.6 *v* 8.0 months) in patients with advanced or recurrent HER2-positive uterine serous carcinoma, a rare type of EC.[19] Results from the current study showed a marked increase in HER2 testing after 2018, coinciding with the incorporation of trastuzumab plus carboplatin-paclitaxel as the preferred treatment for HER2-positive uterine serous carcinoma in clinical practice guidelines.[20]

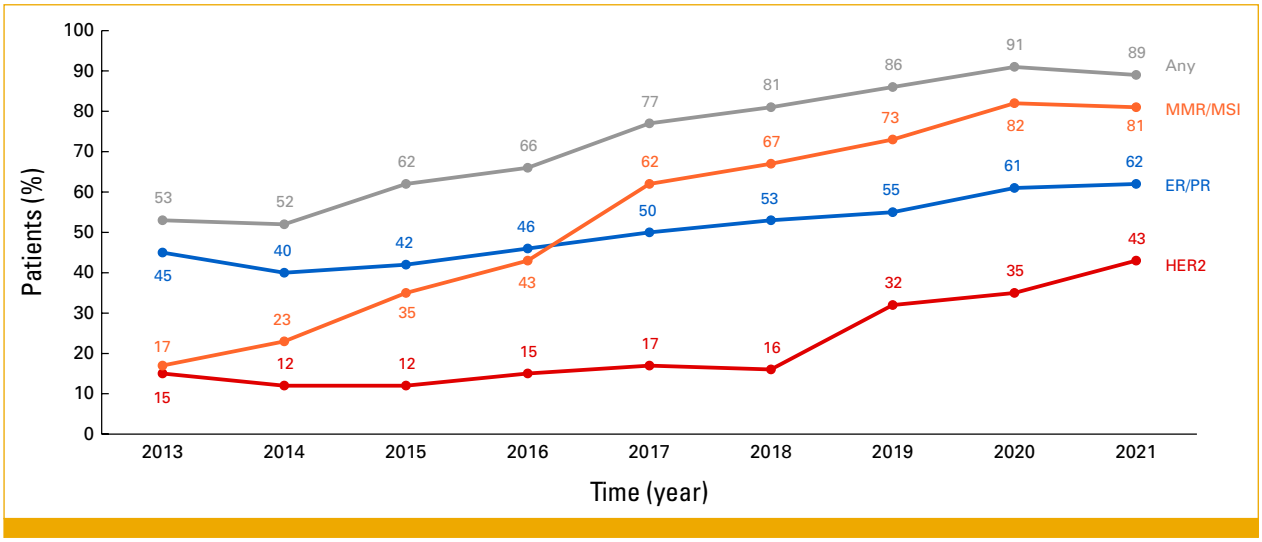

FIG 1. Biomarker testing rates over time for the full EHR data set. EHR, electronic health record; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; MMR, DNA mismatch repair; MSI, microsatellite instability; PR, progesterone receptor.

Several additional studies in pA/rEC have evaluated outcomes in patients with specific biomarkers. In part 1 of the RUBY trial (ClinicalTrials.gov identifier: NCT03981796), dostarlimab plus carboplatin-paclitaxel significantly improved PFS (median PFS, not estimable *v* 7.7 months; $P < .0001$) and overall survival (OS; median OS, not reached [NR] *v* 31.4 months; nominal $P = .0002$) versus carboplatin-paclitaxel alone for patients with dMMR/MSI-H disease.[21,22] In the overall population, PFS and OS benefit was also observed for dostarlimab plus carboplatin-paclitaxel versus carboplatin-paclitaxel alone (median PFS, 11.8 *v* 7.9 months; $P < .0001$; median OS, 44.6 *v* 28.2 months; $P = .002$).[21,22] To our knowledge, these results were the first report of statistically significant benefit in OS overall and substantial OS benefit in the dMMR population, highlighting the need for biomarker testing in these patients. Similarly, in the NRG-GY018 trial (ClinicalTrials.gov identifier: NCT03914612), the addition of pembrolizumab to carboplatin-paclitaxel resulted in a significant prolongation of PFS in the dMMR population versus carboplatin-paclitaxel alone (median PFS, NR *v* 7.6 months; $P < .001$).[23] In the DUO-E trial (ClinicalTrials.gov identifier: NCT04269200), durvalumab plus carboplatin-paclitaxel versus carboplatin-paclitaxel alone demonstrated PFS benefit in the overall population (median PFS, 10.2 *v* 9.6 months; $P = .003$) and for those with dMMR disease (median PFS, NR *v* 7.0 months; prespecified exploratory subgroup analysis).[24]

Positive outcomes of these clinical trials have led to US Food and Drug Administration approvals of targeted therapies in EC. Dostarlimab in combination with carboplatin-paclitaxel followed by single-agent dostarlimab was approved in July 2023 for the treatment of pA/rEC that is dMMR (as determined by an FDA-approved test) or MSI-high[25]; the indication was expanded in August 2024 to include all patients with pA/rEC.[26,27] Durvalumab in combination with carboplatin-paclitaxel followed by single-agent durvalumab was approved in June 2024 for the treatment of pA/rEC that is dMMR only.[28,29] Trastuzumab deruxtecan was approved in April 2024 for the treatment of unresectable or metastatic HER2-positive (IHC 3+) solid tumors, including ECs, that were previously treated systemically and have no

TABLE 2. Biomarker Testing Type and Results in the Full EHR Data Set

Biomarker	Full EHR Data Set (N = 2,982)[a]
HER2, No. (%)	612 (21)
Equivocal	66 (11)
Negative	449 (73)
Positive	75 (12)
Unknown[b]	22 (4)
MMR/MSI, No. (%)	1,604 (54)
Equivocal	NR[c]
Loss of MMR protein expression (MMR protein deficiency)	369 (23)
MSI-ambiguous	NR[c]
MSI-high	38 (2)
MSI-low	NR[c]
MSS	211 (13)
Normal MMR protein expression	902 (56)
Unknown[b]	77 (5)
ER/PR, No. (%)	1,465 (49)
Indeterminate result	NR[c]
Negative	288 (20)
Positive	1,129 (77)
Unknown	47 (3)

Abbreviations: EHR, electronic health record; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; MMR, DNA mismatch repair; MSI, microsatellite instability; MSS, microsatellite stable; NR, not reported; PR, progesterone receptor.

[a]Percentages are testing rates among all patients and result rates among patients who received testing.

[b]Included pending, unknown, and unsuccessful/indeterminate tests.

[c]The number of patients was not reported because of a sample size of ≤5.

	OR	95% CI	*P*	OR (95% CI)
Age, years	1.00	0.99-1.01	.64	
Practice type				
Academic	Ref			
Community	0.59	0.47-0.73	<.01	
Race and ethnicity				
Non-Hispanic White	Ref			
Asian	1.43	0.75-2.73	.28	
Black or African American	0.93	0.72-1.22	.61	
Hispanic or Latino	0.76	0.54-1.07	.12	
Other race	1.32	0.87-1.99	.20	
Unknown	1.09	0.85-1.38	.51	
Insurance status[a]				
Medicare/Medicaid	Ref			
Commercial	1.51	1.18-1.93	<.01	
Other	1.81	1.13-2.90	.01	
ECOG PS				
0-1	Ref			
2+	1.14	0.83-1.57	.43	
Unknown	0.52	0.42-0.64	<.01	
Recurrent *v* primary advanced EC				
Recurrent EC	Ref			
Primary advanced EC	1.45	1.03-2.06	.03	
Tumor grade				
Well differentiated	Ref			
Moderately differentiated	0.83	0.64-1.09	.18	
Poorly differentiated or undifferentiated	0.89	0.66-1.20	.44	
Unknown	1.05	0.71-1.57	.79	
Histology				
Nonendometrioid carcinoma	Ref			
Endometrioid carcinoma	1.39	1.01-1.93	.05	
Lymphovascular invasion				
Yes	Ref			
No/unknown	0.92	0.74-1.14	.44	
Myometrial invasion				
Yes	Ref			
No/unknown	0.86	0.68-1.08	.19	
Previous surgery for the primary treatment				
Yes	Ref			
No	2.29	1.83-2.86	<.01	
Previous radiotherapy as part of primary treatment				
Yes	Ref			
No	0.75	0.49-1.16	.20	

FIG 2. Factors associated with receipt of biomarker testing in the full EHR data set. Testing includes any of the following biomarkers: HER2, MMR/MSI, and ER/PR. [a]Note that Medicare Advantage, Medicare Supplement, Medicare Part D, Managed Medicaid, and Managed Government plans are generally offered by commercial payers and are (continued on following page)

FIG 2. (Continued). captured in the Commercial insurance category. The Other insurance category included self-pay, workers' compensation, other government program, and patient assistance program. EC, endometrial cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; EHR, electronic health record; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; MMR, DNA mismatch repair; MSI, microsatellite instability; OR, odds ratio; PR, progesterone receptor.

satisfactory alternative treatment options.[30] Despite label expansions, patients will likely continue to undergo biomarker testing to help guide treatment planning. This is especially important for MMR/MSI testing because of the potential association with other genetic conditions, such as Lynch syndrome.[31]

Several factors associated with an increased likelihood of biomarker testing were identified in both data sets. In the full EHR data set, patients who received testing were characterized by sicker health status (eg, lymphovascular invasion and/or higher ECOG PS), more advanced cancer at diagnosis, and no previous surgery or radiation as part of the primary treatment. Patients with commercial insurance and those who received care at an academic facility were also more likely to receive biomarker testing. Multivariate logistic regression analysis supported several of these trends. Receipt of biomarker testing before surgery is an encouraging trend that indicates more patients have test results available to aid in decision making before systemic treatment initiation. These findings are consistent with previous reports in other disease areas where testing rates were higher for patients with commercial insurance compared with those with Medicare/Medicaid insurance.[11,32,33] These trends may be attributed to differential access and equity in receiving biomarker testing, including differential reimbursement amounts covered by Medicare/Medicaid versus commercial insurance. Insurance has been previously identified as an important factor in dictating the probability of testing and cancer care that patients receive.[11,34] Inconsistent Medicare/Medicaid policies and a lack of timely updated coverage policies may be other potential explanations for testing rate variability.

Despite guidelines and evidence for its clinical benefit, biomarker testing and the use of related therapies have been accompanied by disparities in patient access and implementation at the provider and institution levels. Lower access to testing may lead to fewer opportunities for biomarker-driven therapies, indicating other potential access barriers to treatments.[11] For example, low access to new technologies such as NGS testing was observed in Medicare/Medicaid patients with colorectal cancer.[11] Receipt of treatment at an academic facility was a predictor for increased biomarker testing likelihood in other disease areas.[11,32,35,36] Biomarker testing may be more likely at academic facilities because of research studies, availability of specialized resources to conduct testing, and clinical trial involvement.[32] In a recent survey, oncologists at academic centers were more likely to order biomarker testing at the time of initial biopsy than oncologists in community cancer programs (76% *v* 52%; $P = .02$) and involve the patient's family in biomarker testing discussions (85% *v* 59%; $P = .009$).[35] As most US patients with cancer are treated in community settings,[12] addressing methods to increase compliance with biomarker testing in community cancer programs is crucial.

Increased biomarker testing for patients with advanced or recurrent EC may improve patient outcomes by identifying targeted treatments compared with nontargeted, conventional

TABLE 3. Test Timing for the Full EHR Data Set

	HER2 (n = 612)		MMR/MSI (n = 1,604)		ER/PR (n = 1,465)	
Timing	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)
Time from diagnosis to test collection date, days	28.4 (39.1)	16.5 (0-38)	25.9 (35.4)	16.0 (0-38)	15.7 (30.5)	0 (0-22)
Time from testing result to treatment initiation, days	74.7 (84.5)	40.0 (25.0-74.7)	88.6 (90.0)	50.0 (29.0-118.3)	81.7 (83.5)	50.0 (29.0-96.8)
Chemotherapy	53.9 (61.4)	34.0 (NR)	63.3 (65.0)	42.0 (NR)	65.1 (66.3)	44.0 (NR)
Immunotherapy	154.3 (167.2)	153.0 (NR)	217.5 (94.3)	257.0 (NR)	216.9 (101.9)	257.0 (NR)
Targeted therapy	207.0 (36.2)	203.0 (NR)	225.3 (59.3)	230.0 (NR)	212.8 (38.5)	226.5 (NR)
Hormone therapy	134.5 (118.8)	84.0 (NR)	153.2 (119.7)	150.0 (NR)	125.4 (111.6)	83.5 (NR)
Combination therapy	103.1 (102.4)	55.0 (NR)	142.3 (111.9)	103.0 (NR)	121.7 (101.4)	77.5 (NR)
Time from diagnosis to treatment initiation, days						
Tested	87.1 (87.2)	56.0 (28-99)	100.1 (93.3)	64.0 (33-128)	89.9 (86.8)	57.0 (32-110)
Untested	95.1 (89.2)	60 (34-123)	83.8 (82)	53 (29-102)	97.3 (91.6)	63 (33-124)

Abbreviations: EHR, electronic health record; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; MMR, DNA mismatch repair; MSI, microsatellite instability; NR, not reported; PR, progesterone receptor; SD, standard deviation.

treatments. One study examining cancer survival found that those with commercial insurance (non-Medicare) had a higher risk of mortality, ranging from 11% to 25%, across different cancers.[37] Future studies are needed to understand whether survival may differ for patients with EC with Medicare/Medicaid compared with those with commercial insurance in the era of precision medicine.

With the increased availability of biomarker testing for EC, it is important to understand the timing of testing. In this analysis, the median time between the receipt of biomarker testing and systemic treatment initiation (40-50 days) was consistent with clinical practice, since most patients who undergo surgery and require adjuvant systemic therapy need to wait ≤6 weeks to initiate treatment. Therefore, biomarker testing performed at diagnosis may lead to improved outcomes, as surgery is generally the primary treatment for most patients, followed by systemic therapy.[17] Timely biomarker testing and initiation of appropriate targeted treatment may affect patient outcomes.[38]

This study has limitations. We were not able to evaluate testing rates for all emerging biomarkers in EC; in particular, *BRCA1/2* mutations and *NTRK* fusions have been reported to be potentially actionable and would therefore be relevant.[17,39-41] Additionally, our study outcomes were not validated because patient records are deidentified. Because EHR data were collected as part of routine clinical care and used in research for secondary purposes, not all testing or treatment information, including test result dates, was available for analysis. If patients did not have an existing specimen collection date for a biomarker test, it was assumed that they did not receive the test. Moreover, with the databases used for this study, it was not possible to see earlier testing data (eg, at initial diagnosis) for the patients included in the analysis. The EHR databases were predominantly sourced from commercially insured plan members and may not be generalizable to other populations, such as those insured by Medicare/Medicaid or with no insurance. In the advEndo Spotlight data set, the median time from diagnosis to treatment initiation represents an unadjusted comparison, and the results should be interpreted with caution. Additionally, the proportion of patients who had surgery for the primary treatment may be relatively low, possibly because of unrecorded surgery in the EHR or surgery conducted at facilities outside of the network. This observation aligns with findings from a previous study of pA/rEC in which 40% of patients had missing surgery information.[42]

This analysis represents a real-world pattern of biomarker testing among patients with advanced EC in the United States over a period of 10 years; it addresses a key gap in our understanding of the factors associated with the utilization of molecular tests in patients with pA/rEC. These results may have implications for both identifying approaches to increase access to testing and leveraging actionable biomarkers to inform appropriate treatment decisions.

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